# HANDBOOK
# OF
# DISEASES OF THE SKIN

by

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*WITH 1057 ILLUSTRATIONS*

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# PREFACE

The brevity and practicality at which I aimed in our *Synopsis of Diseases of the Skin* are also aims of this volume which is intended to supply a text useful to medical students practitioners and specialists in dermatology The medical student who knows a good deal of what is presented here in larger type will be better instructed in dermatology and syphilology than most medical students are Practitioners seeking help in the interpretation and management of a case will profit from the illustrations the prescriptions and some of the material in smaller type. The scholar will find the volume comprehensive for I have held to the policy of at least mentioning almost everything and have included many thousands of bibliographic entries which enable one to find one s way about in the specialistic literature These may be welcome even to the dermatologist certified as learned, whose memory however disciplined is unlikely to bear the burden of retaining everything at all times. This *Handbook* is more complete than our *Synopsis* and is less voluminous than the fourth edition of our *Introduction to Dermatology*

Reviews of previous books of ours have received earnest deliberation, and the constructive criticisms have been adopted where they have not conflicted with the necessarily limited size of the book, or with each other or with my desires That I have colored the pages with personal views will please some readers and annoy others whose tastes or convictions differ from mine

The order of presentation has been altered, with causation the principal guide to classification in the hope that it will appear logical to nondermatologists who have tended with justification to think of dermatology as having possessed hitherto to some extent, a language set apart from those of other sciences. I persist in wishing to tie descriptions and concepts of disorders of the skin with general medicine and biology as I wrote in 1938 in the preface of the tenth edition of our *Diseases of the Skin*

Illustrations numbering in excess of a thousand, have been carefully selected, trimmed, placed, and titled, their legends in appropriate instances giving the author and journal of their original publication.

References, abbreviated to their minimal consumption of space have been incorporated within the textual material, where a reader can learn quickly to skip them or an investigator can use them immediately to find sources and elaborations of thoughts which have been trimmed, like the illustrations, to their essentials Abbreviations of bibliographic references are on pages xi, ff

The index should be pointed out as a source of a variety of information and guidance especially under such titles as Disease Prescription, Syndrome and Test

I would call attention to the technic of the treatment of contact dermatitis by elimination of all possible causes so that the patient is soon relieved, subsequently identifying the actual cause by systematic increment of the patient s chemical environment. This is original and effective A practical technic is presented of detecting ingested allergens

for the relief of urticaria for which I am indebted to my associate, Bernard H Winston, M.D The section on syphilis is consistent with the literature available through the time of completing the galley proof. The presentation of acne vulgaris as a pustular lipidosis has been modified only in details after twelve years of application have failed to disturb my belief in the veracity of my views on its interpretation and treatment. Psychosomatic aspects of dermatology have received consideration. Disturbances of growth comprise a chapter which pleases me.

Hermann Pinkus, M.D supplied us with beautiful photomicrographs of normal adult and fetal skin, and largely from his collection is drawn the noteworthy illustrative material of the chapters on Anatomy and Embryology

Debts to others have been given meticulous acknowledgment throughout the text. I would also acknowledge indebtedness and express gratitude to many individuals who personally have helped me. Charles R. Rein M.D., contributed expositions of the technic of serologic tests for syphilis. E. V Allen M.D., allowed me to reprint material from *Peripheral Vascular Diseases* by himself and collaborators. Oswaldo G Costa M.D., L. Halberstaedter M.D Harry M Robinson, M.D., Harry M Robinson Jr., M.D and Edward A. Gall, M.D., are among those whom I wish also to thank for pictures. Stephen Epstein, M.D reviewed the section on staphylococcic infections in the skin. Bernard H Winston M.D., Norman D Ascl, M.D Herbert Siesener M.D Frank Dwyer M D Jeannette Carter Ph D Rosellen Kissinger R.N Corinne Gallup Hazel Hill, and Nadine Houston protected me from avoidable pressure of medical practice, relief from which was essential to the accomplishment of medical writing Miss Hill indefatigably transformed manuscript from illegible to legible form Dr Winston painstakingly sought out with me the typographic errors in the page proof Miss Opal Woodruff, Librarian, University of Kansas Medical Center and Mr Park Crawford, Acting Librarian, Jackson County Medical Society gave me expert and cheerful assistance.

The advisory capacity of Richard L Sutton, Sr has continued since his retirement in 1935 from medical writing and in 1940 from medical practice. His influence on the manner of thinking herein exemplified is more significant than would have been his contribution of a factual trifle here and there. His senior authorship is to be acknowledged, for he caused me to inherit a book, which is a responsibility and he taught me to try to cure people.

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## CONTENTS

# ABBREVIATIONS OF BIBLIOGRAPHIC REFERENCES

| | |
|---|---|
| A | Archives (of) |
| abs | Abstracted in |
| ActaD-V | Acta dermato-venereologica |
| ADisChild | Archives of Disease in Childhood |
| ADS | Archives of Dermatology and Syphilology |
| AfDuS | Archiv für Dermatologie und Syphilis |
| AfpathAnat | Archiv für pathologische Anatomie |
| AIntM | Archives of Internal Medicine |
| AmHJ | American Heart Journal |
| AmJAnat | American Journal of Anatomy |
| AmJCa | American Journal of Cancer |
| AmJClPath | American Journal of Clinical Pathology |
| AmJDigD | American Journal of Digestive Diseases |
| AmJDisChild | American Journal of Diseases of Children |
| AmJMSc | American Journal of the Medical Sciences |
| AmJOG | American Journal of Obstetrics and Gynecology |
| AmJOphth | American Journal of Ophthalmology |
| AmJP | American Journal of Pathology |
| AmJPubH | American Journal of Public Health and the Nation's Health |
| AmJR | American Journal of Roentgenology and Radium Therapy |
| AmJS | American Journal of Syphilis, Gonorrhea and Venereal Diseases |
| AmJSurg | American Journal of Surgery |
| AmJTropM | American Journal of Tropical Medicine |
| AmM | The American Journal of Medicine |
| AmRevTuberc | American Review of Tuberculosis |
| AnatRec | Anatomical Record |
| ANeurP | Archives of Neurology and Psychiatry |
| AnnAllergy | Annals of Allergy |
| AnndeD | Annales de dermatologie et de syphiligraphie |
| AnnIntM | Annals of Internal Medicine |
| AnnSurg | Annals of Surgery |
| AOphth | Archives of Ophthalmology |
| AOtol | Archives of Otolaryngology |
| APath | Archives of Pathology |
| APed | Archives of Pediatrics |
| APhysM | Archives of Physical Medicine |
| APhysTh | Archives of Physical Therapy |
| ASurg | Archives of Surgery |
| BeitrzKlinChir | Beiträge zur Klinische Chirurgie |
| BiolRev | Biological Reviews |
| BHeartJ | British Heart Journal |
| BJChildDis | British Journal of Childhood Diseases |
| BJD | British Journal of Dermatology and Syphilis |
| BJExpP | British Journal of Experimental Pathology |
| BJOphth | British Journal of Ophthalmology |
| BJPhysM | British Journal of Physical Medicine and Industrial Hygiene |
| BJRadiol | British Journal of Radiology |
| BJS | British Journal of Surgery |
| BJVD | British Journal of Venereal Diseases |
| BMBull | British Medical Bulletin |
| BMJ | British Medical Journal |
| BSocfrancD | Bulletin de la société française de dermatologie et de syphiligraphie |
| BullJHH | Bulletin of the Johns Hopkins Hospital |
| BullNYAM | Bulletin of the New York Academy of Medicine |
| BullUSAMD | Bulletin of the United States Army Medical Department |
| CalifM | California Medicine |
| CalWM | California and Western Medicine |
| CanadMAJ | Canadian Medical Association Journal |
| CanadPHJ | Canadian Journal of Public Health |
| CaRes | Cancer Research |
| ChinMJ | Chinese Medical Journal |
| Clin | Clinica |

| | |
|---|---|
| ClinSc | Clinical Science, Incorporating Heart |
| CurMDig | Current Medical Digest |
| DmedWchn | Deutsche medizinische Wochenschrift |
| DWchn | Dermatologische Wochenschrift |
| DZtsch | Dermatologische Zeitschrift |
| EAfrMJ | The East African Medical Journal |
| EdinMJ | Edinburgh Medical Journal |
| Edit | Editorial |
| Endocr | Endocrinology |
| FlaMAJ | Journal of the Florida Medical Association |
| Geriat | Geriatrics |
| IllMJ | Illinois Medical Journal |
| IndJMRes | Indian Journal of Medical Research |
| IndMGaz | Indian Medical Gazette |
| IndustM | Industrial Medicine |
| InternatClin | International Clinics |
| InternatJLepr | International Journal of Leprosy |
| IowaSMSJ | Journal of Iowa State Medical Society |
| J | Journal of the American Medical Association |
| JAllergy | Journal of Allergy |
| JAmDentA | Journal of the American Dental Association |
| JAnat | Journal of Anatomy |
| JapJD | Japanese Journal of Dermatology |
| JB&JSurg | Journal of Bone and Joint Surgery |
| JBact | Journal of Bacteriology |
| JBiolChem | Journal of Biological Chemistry |
| JClEndocr | Journal of Clinical Endocrinology |
| JClinInv | Journal of Clinical Investigation |
| JCutD | Journal of Cutaneous Diseases |
| JExpM | Journal of Experimental Medicine |
| JHyg | Journal of Hygiene |
| JImm | Journal of Immunology |
| JIndianaMA | Journal of the Indiana State Medical Association |
| JIndustHyg | Journal of Industrial Hygiene and Toxicology |
| JInfectD | Journal of Infectious Diseases |
| JInvD | Journal of Investigative Dermatology |
| JKansMS | Journal of Kansas Medical Society |
| J Lancet | Journal Lancet |
| JLaryng | Journal of Laryngology and Otology |
| JLCM | Journal of Laboratory and Clinical Medicine |
| JMAGa | Journal of Medical Association of Georgia |
| JMichSMS | Journal of the Michigan State Medical Society |
| JMoSMA | Journal of the Missouri State Medical Association |
| JMRes | Journal of Medical Research |
| JMSocNJ | Journal of the Medical Society of New Jersey |
| JNatlCancInst | Journal of the National Cancer Institute |
| JNervMentDis | Journal of Nervous and Mental Disease |
| JObGBE | Journal of Obstetrics and Gynaecology of the British Empire |
| JOklaMA | Journal of Oklahoma State Medical Association |
| JPathBact | Journal of Pathology and Bacteriology |
| JPed | Journal of Pediatrics |
| JPhExpT | Journal of Pharmacology and Experimental Therapeutics |
| JPhys | Journal of Physiology |
| JRoyAMC | Journal of the Royal Army Medical Corps |
| JTennMA | Journal of the Tennessee State Medical Association |
| JTropM | Journal of Tropical Medicine and Hygiene |
| JUrol | Journal of Urology |
| KlinWchn | Klinische Wochenschrift |
| KyMJ | Kentucky Medical Journal |
| Laryng | Laryngoscope |

| | |
|---|---|
| MAnnDC | Medical Annals of the District of Columbia |
| MCNAm | Medical Clinics of North America |
| Med | Medicine, Analytical Reviews of General Medicine Neurology and Pediatrics |
| MJ&R | Medical Journal and Record |
| MJAustral | Medical Journal of Australia |
| MinnM | Minnesota Medicine |
| MP&Circ | Medical Press and Circular |
| MRec | Medical Record |
| MTimes | Medical Times |
| NCarolMJ | North Carolina Medical Journal |
| NebrSMJ | Nebraska State Medical Journal |
| NEngJM | New England Journal of Medicine |
| NOrlMSJ | New Orleans Medical and Surgical Journal |
| NoWM | Northwest Medicine |
| NYSJM | New York State Journal of Medicine |
| OhioSMJ | Ohio State Medical Journal |
| OklaSMAJ | Journal of the Oklahoma State Medical Association |
| PaMJ | Pennsylvania Medical Journal |
| Parasit | Parasitology |
| PHRpts | Public Health Reports |
| PhysRev | Physiological Reviews |
| PIMChi | Proceedings of the Institute of Medicine of Chicago |
| Pract | Practitioner |
| ProcRoySocM | Proceedings of the Royal Society of Medicine |
| PSExpB | Proceedings of the Society for Experimental Biology and Medicine |
| PSMMC | Proceedings of the Staff Meetings of the Mayo Clinic |
| PsychosomM | Psychosomatic Medicine |
| QJM | Quarterly Journal of Medicine |
| QMN | Queries and Minor Notes, in the Journal of the American Medical Association |
| Radiol | Radiology |
| RevMMex | Revista de medicina y ciencias afines |
| RhodeIsIMJ | Rhode Island Medical Journal |
| RMtMJ | Rocky Mountain Medical Journal |
| SCNAm | Surgical Clinics of North America |
| SGO | Surgery Gynecology and Obstetrics |
| Sc | Science |
| SMJ | Southern Medical Journal |
| SM&S | Southern Medicine and Surgery |
| SouthSurg | The Southern Surgeon |
| SouthwestM | Southwestern Medicine |
| Surg | Surgery |
| TexasSJM | Texas State Journal of Medicine |
| UCutRev | Urological and Cutaneous Review |
| USNMBull | United States Naval Medical Bulletin |
| VaMMonth | Virginia Medical Monthly |
| VDI | Journal of Venereal Disease Information |
| WarM | War Medicine |
| WDTBM | War Department Technical Bulletin, Medicine, Washington, D. C. |
| WestJSOG | The Western Journal of Surgery Obstetrics and Gynecology |
| WienMWchn | Wiener Medizinische Wochenschrift |
| WiscMJ | Wisconsin Medical Journal |
| YaleJBiol | Yale Journal of Biology and Medicine |
| YBD | Year Book of Dermatology and Syphilology Year Book Publishers |
| YBPath | Year Book of Pathology Year Book Publishers, Chicago |
| ZfBakt | Zeitschrift für Bakteriologie |

HANDBOOK OF DISEASES OF THE SKIN

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## ANATOMY

The skin is a soft, flexible, membranous covering which completely invests the body and is continuous at the natural orifices with the mucous membranes. Essentially it consists of (1) a connective tissue frame, incorporating blood vessels, lymph vessels, and nerves, comprising the dermis, and (2) an epithelial covering the epidermis. Dermis is that which becomes leather when skin is tanned. Epidermis is that which forms the cap of a blister

The skin ranges considerably in thickness and consistency on various parts of the body It is the largest organ of the body weighing three times as much as the liver It serves principally in protection, heat regulation, sensation, and secretion. It is attached loosely or firmly to underlying structures so as to resemble a closely fitting, elastic garment. Its area averages 16 000 to 18,500 cm. and its weight 3 000 to 3,500 gm. (Leider J 134 1565 1947)

Superficially the skin is marked by tiny wrinkles and furrows. Underlying glands communicate with the surface through pores. On the palms and soles occur parallel ridges corresponding to rows of underlying dermal papillae. The color of the skin is determined by melanin pigment in the epithelium, by carotene, and by blood in the dermal capillaries.

Subcutaneous tissue is composed mainly of adipose lobules. It unites a regular surface with the deep fascia covering muscle and bone, and forms a resilient base for the overlying skin. Lobules of adipose tissue are latticed by an areolar fibrous network which supports blood vessels and nerve trunks. Thickness of the adipose layer was investigated by Stuart and Sobel (JPed 28 637 1946) Fat is an important but ill understood special tissue and storehouse (Wells PIMChi 18 26, 1940)

Lines of cleavage result from the disposition of collagenous bundles under the influence of tension and, in general, parallel the natural creases and the direction of the hair roots (Cox BJS 29 234, 1941)

**Epidermis.**—This ectodermal investment consists of cornifying stratified squamous epithelium. It is apposed to the papillated surface of the underlying specialized mesodermal structure, the corium, or dermis. The basal membrane is the adhesive substance conjoining epidermis and dermis and behaves like a collagen jel for separation of epidermis from dermis is effected by acids and bases at those hydrogen ion concentrations which cause swelling of gelatin (Felsher JInvD 8 35 1947) Agents which swell these hydrophilic colloids, including NaSCN and NaI, decrease their cohesiveness, a fact which may explain their influence on dermatitis herpetiformis. Shrinking agents include $Na_2SO_4$ and Na citrate in 2N concentration. Karyokinetic division furnishes the layers from within outward. Mitoses occur twice as frequently in the night as during the day (Broders and Dublin PSMMC 14 423 1939) and epidermis of glabrous skin renews itself continuously from within outward in about 7 days, corneous scales flaking off inconspicuously under normal conditions.

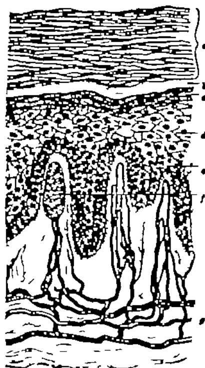



Fig. 1



Fig 2

Fig. 1.—Section of skin, diagrammatic, showing (a) stratum corneum, (b) stratum lucidum, ( ) stratum granulosum, (d) stratum mucosum, ( ) stratum germinativum, (f) neural end organ in a dermal papilla, (g) ascular and neural plexuses in the dermis. (Cunningham Anat my )

Fig. 2.—Section of skin, diagrammatic, howing two coiled sweat glands hair follicle, and a Pacinian corpuscl in their relation to the epidermal, dermal and dipose layers (Cunningham Anat my )



Fig 3 —Normal kin from trunk. (Dr H. Pinkus.)

of disputed structure but probably is fibrillar Nutrient exchange occurs through the medium of tissue juices, for the epidermis is avascular The deep portion of the dermis, the reticular part, consists of dense interlacing bundles of white fibrous tissue and merges beneath with the subcutaneous tissue Slender branching strands of yellow elastic tissue are



Fig. 5.—Epidermis, showing keratinization, granular layer and corneum (Dr H. Pinkus.)

Fig 6 —Skin of digit showing normal corneum, epidermis, and papillary portion of dermis Sweat duct in epidermis is centrally located in the photomicrograph. (Dr H. Pinkus.)



Fig. 7



Fig. 8

Fig. 7.—Skin of chest, elastic fibers stained black. (Dr H. Pinkus.)
Fig 8.—Elastic tissue of papillary layer of dermis. (Dr H. Pinkus.)



Fig. 9



Fig. 10.

Fig. 9.—Connective tissues of normal dermis collagenous bundles, fibrous tissue cells, and small vessels. (Dr H. Pinkus.)

Fig 10.—Arteriole, nerve and venule in deep part of normal dermis. (Dr H. Pinkus.)



Fig. 11.



Fig. 12.

Fig. 11.—Melanin pigment in basal cells of Negro epidermis. (Dr H. Pinkus.)
Fig. 12.—Areola of nipple showing bundles of smooth muscle tissue. (Dr H. Pinkus.)



Fig. 13.



Fig. 14.

Fig. 13.—Injected capillaries of vermilion border of lip. (Dr H. Pinkus.)
Fig. 14.—Injected capillaries of nail bed in transverse section of nail and its bed. (Dr F. G. Harris.)

threaded through it surrounding sebaceous and coil glands, hair follicles, and blood vessels. Larger fibers of elastic tissue are in the deeper part of the dermis, and small fibers form a fine network close beneath the epidermis, but the reticular fibers of the dermoepidermal junction are demonstrably distinct from elastic tissue, according to Dick (JAnat 81 201 1947)

Numerous rounded or conic projections of the papillary layer rest on the dense connective tissue There are about 100 projections to each square millimeter of body surface, totaling some 150 000 000 They are composed of fine bundles of collagenous fibers and contain one or two capillary loops. Medullated and nonmedullated nerve fibers and simple and special nerve endings occur in many of the papillae, particularly in regions where tactile sense is highly developed.

**Pigment.**—The brown hue of the skin is due to an amorphous substance, melanin, present as intracytoplasmic granules in the basal cells of the epidermis and in argyrophile dendritic cells capable of ameboid movement. These dendritic cells, melanophores, occur in the epidermis and also in the dermis. Some of them do not contain melanin but contain precursor oxydase granules demonstrable on treatment with dopa, dioxyphenylalanine, which is changed to melanin (Bloch AFDuS 124 129 1918) Melanin is a chromoprotein, iron free probably a metabolite of pyrocatechol. Pigment production is increased by many forms of irritation and inflammation, the increment being conspicuous in persons capable of generous formation of pigment especially in Negroes. Some kinds of inflammation result in depigmentation. Pigment granules are carried to the epidermis, and they may also be carried from it (Becker ADS 16 259 1927 Clin 3 886, 1944 Edwards and Duntley AmJAnat 65 1 1939)

Carotenoid substances give rise to the yellowish hue.

Blood in the superficial capillaries is the source of the reddish color Dilation of capillaries increases intensity of redness. Compression constriction, collapse, and atrophic diminution in the number of capillaries, and anemia result in pallor

**Lymph Vessels** form a superficial plexus in the papillary part of the dermis, and in the subdermal layer a deep plexus communicates with the trunks which follow the subcutaneous blood vessels. The superficial plexus is so abundant that injections in the lymphatics are absorbed almost immediately While particulate matter is not perfused through the walls, slight trauma causes great increase in permeability as do heat, light, and chemicals also (Hudack and McMaster JExpM 57 751, 1933)

**Blood Vessels.**—A rich supply of blood is maintained by two parallel horizontal systems of vessels, the subpapillary and subcutaneous plexuses. From the superficial plexus, capillary loops extend into the tips of the papillae. Numerous branches of the deep plexus supply the hair follicles, sebaceous glands, and coil glands. (Clark and Clark AmJAnat 64 251 1939)

**Myoarterial Glomus.**—In the pulp of the fingers and toes, the palms and soles, and elsewhere in the body there are special organs which function as arteriovenous anastomoses. In a glomus the afferent arteriole divides as it approaches the surface, part going to the skin, and part by way of a thick walled neuromuscular glomus to a venule These Sucquet Hoyer canals are normal and functional parts of the vascular system, serving to control the aeral circulation.

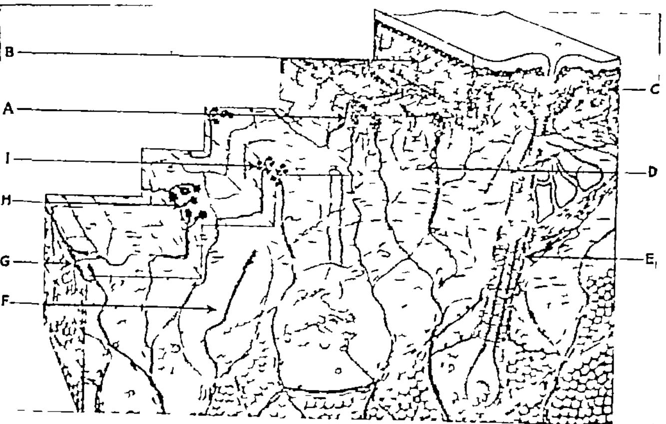



Fig. 15.—Cutaneous innervation, schematic. A, groups of Meissner corpuscles subserving the sensation of touch. B, beaded nerve nets subserving pain (probably fast pain). C, Merkel discs subserving touch. D, beaded nerve fibers derived from nerve nets subserving pain and associated with blood vessels (probably slow pain). E, nerve terminals around the sheath of a hair subserving touch. F, a pacinian corpuscle subserving pressure; G, a group of Ruffini endings subserving warmth. H and I, groups of Krause end-bulbs subserving cold (these lie at somewhat variable depths beneath the skin surface). Note.—The organized endings are accompanied in every instance by fine-beaded nerve fibers subserving pain. (Weddell, BMBull 3: 16, 1945.)

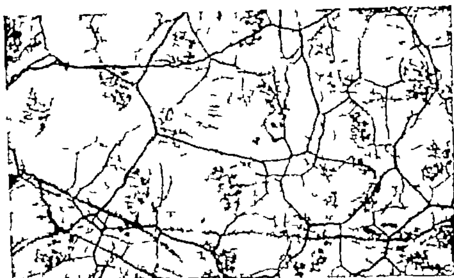


Fig. 16.—Beaded nerve palm-net arising from fine myelinated fibers, seen from above. (Weddell, HMBull 3: 167, 1946.)

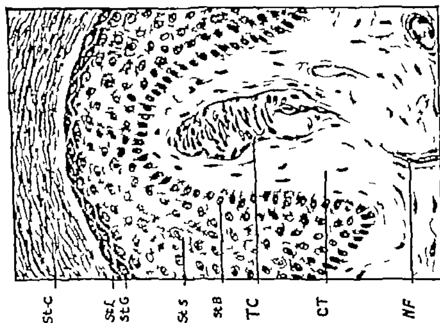



Fig. 17.—Section of palm, Bielschowsky's stain. *TC*, a Meissner tactile corpuscle. *St-C*, is stratum corneum; *St-L*, stratum lucidum; *St-G*, stratum granulosum; *St-S*, stratum spinosum; *St-B*, basal layer of the rete malpighii; *CT*, connective tissue of the pars papillaris; *NF*, a nerve fibril ascending to form the tactile body. (McCarthy: *Histopathology of Skin Diseases*, The C. V. Mosby Co.)

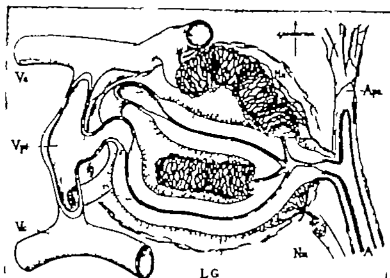



Fig. 18.—Glomus neuromyoarteriovenous anastomotic organ, schematic. A, superficial preterminal artery. Apa, terminal branch entering capillaries. Side branch is afferent artery entering the glomus, dividing into four neuromuscular arterioles. Elastica of afferent arteriole disappears as arteriole enters glomus. Wall of vessel becomes thick due to increase in smooth muscle fibers, which terminate abruptly at beginning of venous segment. Efferent glomic vein leads into a collecting vein (V pd.) which is dilated and thickened at the junction and it leads into superficial vein, V.c. Nn is rich perivascular network of nerves, connected with periarterial sympathetic nerves as well as myelinated sensory nerves (Nm) to the skin. L.G., connective tissue capsule. (After Masson, Oughterson and Tennant, Surg 5 84, 1939.)



Fig. 19.



Fig. 20.

Fig. 19.—Meissner corpuscles in dermal papillae of digital skin. (Dr. H. Pinkus.)

Fig. 20.—Vater-Pacinian corpuscle of finger tip. (Dr. H. Pinkus.)

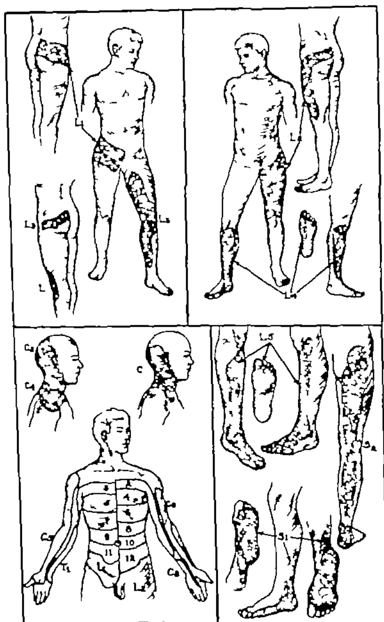



Fig 11.—Sensory innervation of cutaneous regions. Foerster' dermatomes. Not on charts, $C_7$ begins lower on upper arm than $C_6$ and includes most of the hand. $S_3$, $S_4$, and $S_5$ overlap [at] anus and about genitalia. (Fender: ANeurP 41 688, 1938.)



Fig 22.—Axillary skin and apocrine glands. (Dr H. Pinkus.)



Fig. 23.—Apocrine glands from axilla, and myoepithelial cells. (Dr H. Pinkus.)



Fig 24.—Eccrine glands, from forearm. (Dr H. Pinkus.)

Nerves of the skin follow in general the course of the blood vessels. There are medullated and nonmedullated fibers. The main trunks run horizontally in the subcutaneous tissues and give off branches which divide and pass into the dermis with the arteries from the subcutaneous plexus. Slender branches pass into the papillary bodies, and some terminate there in special end organs. Nonmedullated fibrils are distributed to the endothelium of the capillaries and also pass through the papillae, lose their



Fig. 25.—Vulvar sweat glands (Dr H. Plakus.)

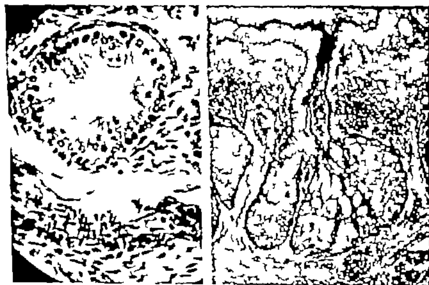


Fig. 26. Fig. 27.

Fig. 26.—Apocrine gland during secretion. (Dr Stuart W y)
Fig. 27.—Sebaceous gland from nose, not associated with a hair

sheaths, and terminate on the cells of the epidermis. Skin innervation is beautifully illustrated in the article of Weddell (BMBull 3 733, 1945). Free sensory endings are often ball or knob-shaped. Merkel has described tactile cells, which are found in the deeper layers of the epidermis, especially numerous in the epithelium of hair follicles. Nevi seem to be collections of anomalous cells of this type (*Ebert ADS 37 1 1938*). Hair follicles receive their nerve supply in a manner similar to that of the epidermis, the fibers passing into the prickle-cell layer of the follicle. Several types of encapsulated nerve endings occur in man the tactile corpuscles, or corpuscles of Meissner the end bulbs of Krause and of Pacini, the genital corpuscles, and the terminal cylinders. The corpuscles of Meissner are small, oval structures from 80 to 150 microns long and about one-half as broad. They are found in sensitive regions the palms, soles, lips, nipples, penis, and clitoris, and dorsums of the hands and feet. They generally occupy the tips of the papillae, their long axes perpendicular to the surface Pacinian corpuscles are not confined to the connective tissue of the skin but are also found in many other parts of the body These bodies are large oval, onionlike structures, which range from 0.5 to 2.0 mm in length. They possess a thick capsule composed of from one to three dozen concentric layers of fibrous tissue and a core of granular semi solid material in which the naked axis cylinder is embedded



Fig. 21.



Fig. 22.

Fig 21—Sebaceous gland. (Dr H. Pinkus.)
Fig. 22—Eccrine gland, elastic tissue stain (Dr H Pink )

Evidence indicates that the end organs of Krause are cold receptors, those of Ruffini are warmth receptors, and those in hair follicles are touch receptors, while free endings mediate painful stimuli. Tactile fibers are myelinated pain and thermal fibers nonmyelinated One nerve fiber carries only one kind of endings (Woollard J Anat 71 54 1936 Zotterman JPhys 95 1 1939 Kuntz and Hamilton AnatRec 71 357 1938) The doctrine of specificity of nerve function is supported clinically physiologically and anatomically (Walshe Brain 65 48 1942) of the 4 primary modes of sensation, touch pain, cold and warmth each is a sensory unit with end organs disposed in the skin in area and in depth such that *activation of a spot influences the whole unit* Pain is the sense mediated by all on extreme excitation The anatomy of cutaneous sensibility was well set forth in an editorial, BMJ 2 342, 1942.

**Nocifensor System.**—It is probably true that there exists in the skin an intrinsic neural system a posterior root system the axones of which arborize freely in the skin. Vascular flares at the sites of injury apparently are due to the vasodilating influence of these nerves, for the flare reflex, normally provoked by pricking the skin through a droplet of histamine solution, *persists only 5 to 7 days after a cutaneous nerve is cut.* The histamine test is useful to test the integrity of cutaneous nerves, as in leprosy. Histamine provokes whealing but not erythema after degeneration of the nerve. (Lewis BMJ 1 431 491 1937 Costello and Tiant ADS 47 826 1943.)



Fig. 30.



Fig. 31.

Fig. 30.—Hair from chest lanugo. (Dr H Pinkus.)

Fig. 31.—Hair longitudinal section, from face, showing hair change. Old hair is at level of sebaceous gland. New papilla is growing deeper (Dr H. Pinkus.)



Fig. 32.



Fig. 33.



Fig. 34.

Fig. 32.—Hair of scalp, growing papilla.

Fig. 33.—Scalp hair cross section at deep level.

Fig. 34.—Scalp hair cross section at superficial level.

**Muscles of the Skin.**—The striated are limited to the superficial voluntary muscles of the face and neck. The nonstriated are abundant, particularly in the scrotal and perineal regions, about the nipples, and in the scalp. Arrector muscles of the hair follicles are bundles of smooth muscle fibers, the contraction of which gives rise to "goose flesh."

**Sweat Glands**, or coil glands, are modified tubular glands which occur on all parts of the body except the margins of the lips, the glans, and the inner surface of the prepuce. They are most numerous on the palms and soles. Anatomically there are two parts, a body and an excretory duct. The body is globular and consists of windings of an epithelial tube of fairly uniform caliber. The secreting or glandular portion of the tubule is composed of a single row of low columnar cells. Their bases rest on a thin layer of myoepithelial cells, the spindle-shaped elements of which are

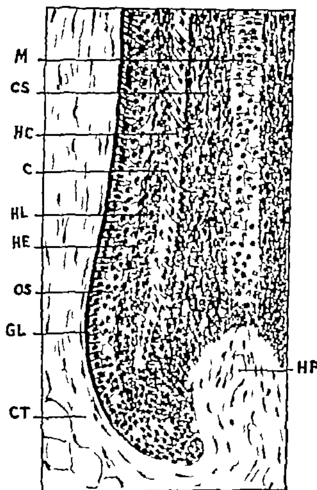



Fig. 31.—Section through lower third of follicle with its hair, hair bulb, and hair papilla. *M* is medulla of hair. *CS*, the cortical substance, rich in pigment granules. *HC*, the cuticle of the hair. *C*, the cuticle of the follicle. *HL*, Huxley layer. *HE*, Henle layer. *OS*, the outer sheath with external row of basal cells. *GL*, the glassy layer of the hair bulb. *HP*, the hair papilla with vessel. *CT*, connective tissue. (McCarthy: *Histopathology of Skin Diseases*. The C. V. Mosby Co.)

arranged longitudinally Surrounding this layer is an external sheath of fibrous and elastic tissue. The glandular portion of the sweat coil is supplied with blood from a network which surrounds it. The nerves consist of nonmedullated sympathetic fibers, which form a close plexus on the outer surface and give off fibrils to the glandular and muscular cells. The duct is a tubule lined with two layers of pavement epithelium. It passes through the dermis in a spiral until it reaches the epidermis, where it loses its connective tissue sheath. In the stratum granulosum it assumes a corkscrewlike course, and opens on the surface Sweat duct epithelium is distinct from the epidermis, although encased in it (Pinkus JInvD 2 175 1939 A.f.exper.Zellforsch. 22 47 1938 tissue culture)

**Apocrine Glands.**—Certain large glands, especially of the pubic circumanal, abdominal, mammary and axillary regions, secrete fatty and odorous substances as well as sweat. They are twice as numerous in the female as in the male. They are more numerous in the Negro than in the Caucasian. They atrophy with advance of age more than ordinary sweat glands. The distal portion of the secretory cell is discharged with secretion, whereas in sebaceous glands the whole cell disintegrates to form the secretory product and in eccrine glands the secretory cell remains intact (Way and Memmesheimer ADS 34 797 1936 38 373 1938)

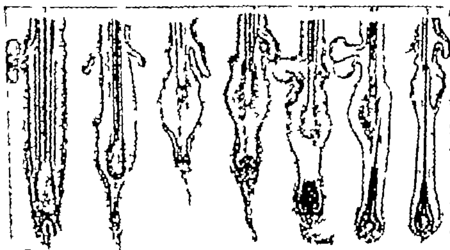


Fig 16.—Regeneration of hair (after Unna) (Pusey Principles and Practice of Dermatology ed. 4, D. Appleton-Century Company)

**Sebaceous Glands** secrete oil These are usually, but not necessarily associated with hair follicles. The Meibomian glands in the eyelids are modified glands of this type as are also the smegma glands of the penis. Sebaceous glands occur on all parts of the body except the palms, soles, and terminal phalanges. A sebaceous gland consists of a fibrous capsule, a membrana propria, and a collection of epithelial elements. The capsule and lining membrane are continuous with the corresponding layers of the hair follicle and the epithelium is a direct prolongation from either the outer root sheath of a follicle or the prickle-cell layer of the epidermis. These organs range from small simple pouchlike alveoli, to large lobular racemose structures. The center of the alveolus is filled with larger

cuboidal or polyhedral cells which undergo fatty degeneration. The epithelial débris escapes into the hair follicle or directly upon the surface of the skin and comprises sebum. Sebaceous glands are responsive to endocrine influence and become larger and more active when androgen is given (Rony and Zakon ADS 48 601, 1943) See Seborrhea, p 398 See histochemical studies of Bunting et al (AnatRec 100 61 1948)

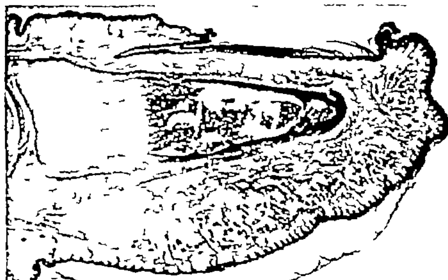


Fig 17—Longitudinal section of digit f premature (Dr H. Pinkus.)

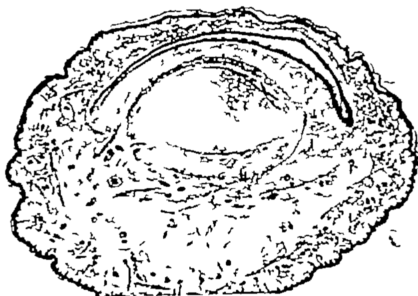


Fig. 18—Transverse section of digit of premat cutting nail pr mal t pr ximal nail fold. (Dr H. Pinkus)

**Hairs** are cylindric, horny structures derived from the epidermis, implanted in pouchlike depressions in the dermis. They occur on all parts of the body except the palms and soles, penis and terminal phalanges. There are 3 classes of hairs: (1) lanugo or fine soft hairs; (2) long hairs, as those on the scalp, pubes, bearded region and axillae; and (3) short, stiff hairs, such as are found on the eyebrows and eyelids. A hair consists of a shaft and a root, which is embedded in the skin. The cortical substance of the shaft is composed of flat nucleated, epithelial cells. The medulla of the shaft is filled with cells which contain more or less pigment. Air spaces are present in both cortical substance and medulla. Externally the shaft is covered with a thin semitransparent, shiny cuticle composed of flat, imbricated cells. On transverse section straight hairs are circular and curly and kinky hairs are elliptical.

**Shedding of Hairs** is normal and continues throughout life. Each hair is exchanged at intervals of several months. When a hair is about to be shed cornification of the root extends down almost to the papilla, the bulb splits into fibrils, the hair separates at the papilla, and the follicle becomes constricted at this point. As the exfoliating hair pushes outward and falls away, a new papilla develops by outbudding from the side of the old follicle. (Pinkus: JInvD 9: 91, 1947.)

**Growth and Distribution of Hair** are little understood. Hypertrichosis is found in hypophysealism, hyperpituitarism, hypergenitalism, and hyperfunction of the cortex of the suprarenal gland. With endocrine disturbances there are striking differences in the growth and distribution of the hair between men and women. Hypopituitarism causes the male to assume the female type of distribution of hair, but it does not cause the female to assume the male type of distribution. Hyperpituitarism, on the other hand, causes the male to become more masculine in type and the female to become masculine in type. Hyperplastic tumor of the cortex of the suprarenal gland also causes the male to become more masculine in type of distribution of hair and the female to assume the masculine type of distribution of hair. Vitamin A and thyroid metabolism are much concerned with hair texture and its degree of dryness or fragility.

**Nails** are flat, horny plates which overlie the ends of the dorsal surfaces of the fingers and toes. They are composed of modified epithelial tissue. The nail root is firmly embedded in the nail groove, a pocketlike recess of the dorsal digital skin. The nail plate is composed of flattened, corneous cells and, together with its underlying epithelium, is supported by the dermal nail bed. The proximal portion, or root, is the productive area of the appendage and is the zone of distad growth. Connective tissue fibers in the subungual region are arranged both vertically and horizontally. Vertical fibers extend from the periosteum to the undersurface of the nail bed and bind the nail firmly in place.

The rate of nail growth varies. It is most rapid in the young and during the summer months. It amounts to about 1.0 mm. per week (Clark and Buxton: BJD 50: 221, 1938).

**Epidermis** is, from an early age, an ectodermal vestment of two layers. The epitrichium, a surface layer of flattened horny cells, corresponds to the corneum of the adult. From a single basal layer which rests on the mesoderm, destined to become dermis, is derived the multilayered epidermis.

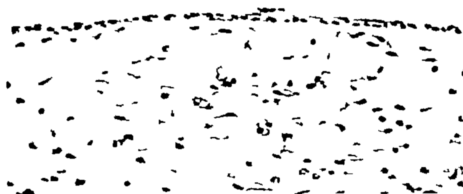


Fig. 39.—Skin of 3-month human embryo. (Dr. H. Pinkus.)



Fig. 40.—Skin of premature, from toe, showing regular pattern of cristae cutis and sweat ducts. (Dr. H. Pinkus.)

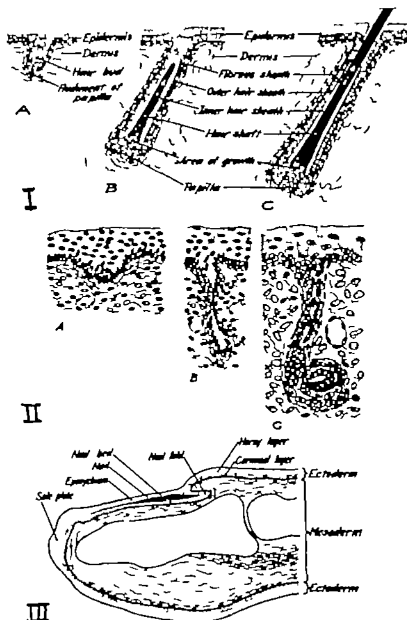



Fig. 41.—I. Development of hair (A) early stage of bud; (B) hair has differentiated within axis of bud and is growing toward surface (C) hair fully developed. II. Stages of development of sweat gland. III. Longitudinal section of nail of fifth month fetus, diagrammatic. (Dodds, G. S. Essentials of Human Embryology John Wiley & Sons, Inc.)



Fig. 4



Fig. 42

Fig. 4 —Hair g rm of 14 1 ) rat fetus (Dr. M garet Murray.)
Fig. 43—H ir germ of 16 1 ) rat fet s. (Dr. M rgaret M rray.)

Fig. 44—Sensory hairs from face of 16-d y rat fetus, ha ing grown 4 days in itro. Follicles ha des loped in the xplanted skin, showing normal topography in vitro, mecha ical obstruction ha ing been oided. The h ir organ is formed by growth and differentiation of groups f cells lready determined as to morphologic nd dynamic potencies. Pigment makes its first ppearance in the epidermis of the hai bulb, just above the dermal papilla. (Dr. M rgaret Murray.)

**Sweat Glands and Hair.**—During the third month, first upon the fingers, palms, and soles, sweat glands grow by downward budding from the epidermis into the dermis. Hairs first become manifest in the eyebrow chin, and upper lip regions at the end of the second month.

**Dermis and Hypodermis** during the first six weeks consist of ordinary mesenchyme. In the second month, fibrillar interstitial substance begins to be produced, elastic fibers appearing later. Soon the mesenchyme divides into a superficial compact layer and a deeper loose one which is to be the subcutaneous portion. The dermis further differentiates into an external papillary layer and a reticular layer in which the collagenous bundles become thick and interlaced.



Fig. 41.—N ll of premature. (Dr H. Pinku )

**Nails** are earliest evidenced as flat areas on the backs of the terminal phalanges during the third month. These primary nail fields are surrounded by a fold, deeper grooved on the proximal side. Not until the fifth month is the true nail substance produced in the proximal nail groove, the deep epidermis being transformed into nail matrix. As the thin nail plate moves distally within the epidermis, the overlying layers are desquamated until the plate is fully exposed, being covered only by the proximal fold.

# PHYSIOLOGY

The skin is the dividing line between the individual and his environment. It is primarily a barrier. It serves in protection, sensation, heat regulation and chemical exchange with the exterior. As an organ of three times the weight of the liver its functions concerned with water, nitrogen, glycogen and vitamin metabolism and with inflammatory and immunologic activities are significant.

**Protection.**—The insensitive, insoluble, fat-covered, and relatively inert horny layer with its underlying regenerative epithelium resists abrasion, light, heat and living organisms and the tough resistant dermis on its springy elastic base of fibrous and adipose tissue admirably absorbs extrinsic forces and displacements. Light is reflected, or absorbed by pigment. Heat is radiated by increased blood flow. Bacteria and yeasts decrease to the extent of 75 per cent in ten minutes and 95 per cent in half an hour on dry healthy skin (Cornbleet and Montgomery, ADS 23, 908, 1931). Self-sterilization depends on drying, acidity, a factor enhanced by ketogenic diet but ill understood, fatty acids of sweat, light and exfoliation (Burtenshaw, BMBull 3 161 1945). The pH of the skin surface of children averaged near 4.0 for all age groups on the scalp, chest and extensor aspects of the forearms, but was higher in the axillae and between the toes (Herrmann et al, JInvD 7 215 1946).

Skin Flora.—Microorganisms of many kinds are found on the skin, but those which constitute the skin flora have little invasive power. Some of them may be able to attack only when mechanical or chemical injury or altered physiologic integrity renders the skin more vulnerable. When a pathogen is present, however, as in furunculosis or infectious eczematoid dermatitis, virulent organisms are available over the whole surface so that a minor abrasion promptly becomes infected. Pathogens may be present transiently, the streptococcus being, it is thought, always either a pathogen or a transient. The dermatophytes are capable of utilizing keratin, despite the fact that it is chemically inactive; this advantage over other fungi forms the basis of their pathogenicity (Benham and Hopkins, ADS 28 532, 1933). Hydration or alkalinization increases the flora, while dehydration or acidification diminishes it (Arnold, JInvD 5 207 1942). In the presence of pyogenic dermatitis, pathogens may be found widespread on noninvolved skin (Martin, BMJ 2 245 1942). See also Pillsbury et al (ADS 45 61 1942), Pillsbury and Nichols (JInvD 7 365 1946), Rebell (ib 8 13 1947).

**Sensation.**—Sensory end organs are distributed over the skin in a punctiform manner. Areas most sensitive to heat and cold are found on the lips, tip of the tongue and eyelids. Pressure points are close to hair follicles, and on nonhairy regions probably depend on the tactile or Meissner corpuscles in the papillae. They are more numerous and smaller than hot and cold points. Pain sense is disseminated generally and is also punctiform in distribution; the free sensory ending is probably its receptive organ. Surface pain is accurately localized. Sensory spots on the skin must be distinguished from end organs themselves, for Gilmer and Haythorn (ANeurP 46 621, 1942) did not find nerve endings under pressure-

vibration spots, and Weddell (JAnat 75 346 441 1941) showed that sensory spots overlie more than one ending or group of endings of the same type and that nerve fibers subserving the spot are separate and multiple. More than one Krause end bulb may hang on one nerve fiber and a terminal network for pain may spread over a circular area almost 1 cm. in diameter Itching and pain are apparently mediated by the same receptors and fibers (Rothman: *The Nature of Itching* Williams and Wilkinson 1943) See also pruritus, p 476 and Bishop (JInvD 11 143 1948)

Referred pain from internal disorders is referred to the region of the surface distribution of the same or adjacent somatic neural segments (see p 11)

Nerve injury which denervates and so diminishes sweating results in increase of electric resistance of the skin, and the mapping of skin resistance may be used to delineate denervated areas accurately (Richter and Katz J 122 648, 1943)

**Chemical Exchange.**—EXCRETION comprises (1) fat from sebaceous glands, (2) sweat, and (3) exfoliation which is continually taking place over the entire surface. The sebaceous secretion, sebum is an oily yellowish semifluid substance mixed at the sebaceous orifices with dirt, bacteria, and frequently *Demodex folliculorum* Accumulating in quantity on the fetus, sebum forms the vernix caseosa. Under the prepuce, mixed with macerated epidermis, it collects as smegma.

Sweat is a clear fluid of low specific gravity (1 004) faintly acid containing mainly sodium chloride some 3 to 40 mg of sugar per 100 c.c., and 0.5 gm. of organic nitrogen in the 500 to 3 000 c.c. secreted daily It also contains a little urea, uric acid, creatinin, ethereal sulfates, and other organic bodies. In uremia chlorides and urea may be deposited in crystals on the skin from dried perspiration See Barney (J 85 1373 1925) Loss of vitamins by sweating, even if profuse, is probably negligible, excepting perhaps niacin (Mickelson and Keys JBiolChem 149 479 1943) Studies of Lobitz and Osterberg (ADS 56 819 827 1947 57 69 387 1948) have indicated that the sweat gland is normally a sugar barrier capable of concentrating urea and perhaps able to form ammonia as the kidney does profuse sweat differs from intermittent sweat in that the former contains no measurable uric acid

ABSORPTION by the skin occurs to a considerable degree. Abrasion greatly increases the absorptive capacity Iodine sprayed on the skin appears in the urine and saliva in 20 minutes. Mercury is effectually administered by inunctions, and vaccines and hormones can be given so. Fats with substances dissolved in them absorb largely through the follicular openings (Eller and Wolff J 114 1865, 2002, 1940 Macht ib 110 409 1938 Rothman: JLCM 28 1305 1943 Mackee et al. JInvD 6 43 1945)

**Heat Exchange** is accomplished by conduction, radiation and evaporation of sweat. This is regulated by nervous activation of the sweat glands and by dilation or constriction of the capillary bed. Heat loss by evaporation depends upon humidity and air movement loss by radiation, upon the external temperature. Emotional tension induces acral vasoconstriction, cooling and hyperhidrosis (Mittelmann and Wolff PsychosomM 1 271 1939 5 211, 1943) The mechanism of heat loss and temperature regulation was discussed by DuBois (AnnIntM 12 389 1938) who emphasized that fact that about 15 kg of tissue is located within 1 cm. of the body surface.

**Temperature.**—Investigations of cutaneous temperature are not of great practical importance in dermatology but they have significance in the consideration of vascular diseases. Normal temperature dependent on environmental and body temperature as well as that of structures immediately underlying, ranges usually between 33.5 and 36.9 C. Obese persons have lower skin temperatures than thin ones. Symmetric areas have about the same temperature differences exceeding 1 C being scarcely normal. The extremities show great variation with environmental changes. If an arm is immersed in hot water the skin of the toes and forehead normally becomes warmer. The failure of the toes to warm up under this condition (used as a test) indicates vascular obstruction of some sort. If the arm is immersed in cold water instead of hot the converse takes place and failure of pedal temperature response means vascular inadequacy. The removal of sympathetic vasoconstrictor influence causes elevation of the temperature of the extremities in vasospastic disease but not in an occlusive vascular disorder. Skin temperature is raised by capillary dilation, lowered by constriction. Active hyperemia induced by irritants or inflammation results in increased warmth (Bierman: J 106: 1158 1936)

**Vascular Activity**—Blood vessels are capillary tubes composed of living endothelium, arterioles venules, and anastomotic channels which possess living muscular and neural tissues as well as endothelium. Blood cells and plasma course through these structures, and they are surrounded by living fibrous tissue cells, motile reticuloendotheliocytes, nerve fibrils and terminations, collagenous and elastic tissues, and epidermal structures. Tissue fluid is the fluid which permeates the tissues, having penetrated capillary walls largely because of capillary blood pressure. It drains into the closed but permeable system of lymph vessels (Drinker AmHJ 18 389 1939)

Vascular response to stroking the skin consists in capillary vasodilation due to the release of a histamine like (H ) substance. Such vasodilation appears within 15 seconds, is maximum in 45 seconds, and fades gradually. A flare of redness extends beyond the line of stroking if the stimulus is sufficiently strong and is apparently due to arteriolar dilation. The flare depends on integrity of the cutaneous nerves. A wheal results from severe stimuli or in abnormally susceptible skins even upon mild stroking, and is due to increase of permeability of the capillaries and transudation of fluid. Normal capillary blood pressure approximates 20-40 mm. Hg. The application of a tourniquet raises this pressure and Lewis and Harmer (Heart 13 337 1926) found that a pressure of 90 mm lasting 3 minutes fails to cause rupture of the walls in normal persons. Excessive fragility can be determined by a tourniquet test and is significant in the study of purpura.

**Inflammation** is a function of living tissues. Various cellular and humoral responses are physiologic responses to various kinds of insult physical chemical, or parasitic. Cells have limited capabilities, and the skin can respond in only a limited assortment of ways. Comprehension of inflammation both from gross and microscopic standpoints, and a view of it as an activity with a time dimension are fundamental to the understanding of inflammatory disease of the skin as well as of other organs. The student should have gained this from basic science instruction prior to embarking upon dermatology but nowhere else is inflammation more readily observed. Guiding references include Aschoff (*Lectures on Pathology* Hoeber 1924) Rich (APath 22 228 1936) Menkin (JExpM 67 145 153, 1938 Sc 101 422, 1945 ib 105 538 1947 *Dynamics of Inflammation* Macmillan 1940)

The investigations of Sabin and Joyner (JExpM 68 659 837 1938) and many others, concerning the histologic responses of the skin to materials injected intracu-

taneously constitute the connecting link between discussions of immunity and pathology. The inflammatory reaction inhibits the dissemination of bacteria at that site. Fixation locally is effectual for foreign animal protein if the body contains specific precipitin for that protein. *Fixation is largely dependent on the early outpouring of fibrin*, for this precedes the appearance of cellular inflammatory response. Menkin was confident that the localization or spread of a given bacterium which had been introduced into the skin is significantly determined by its ability to incite fibrinous exudation and thrombosis of local lymphatics. An extract from exudates, also found in serum digested by trypsin, is capable of initiating the basic sequences of inflammation, increasing the permeability of capillaries, causing swelling of the endothelium, and *provoking the migration and perivascular infiltration of polymorphonuclear leucocytes.* Menkin (1938) crystallized this substance, showed that it contains nitrogen, and named it leukotaxine.

Some inflammatory lesions resolve completely; others leave a residue of fibrosis or atrophy. Pigmentation is usually altered, temporarily enhanced or reduced.

Diffusible substances are absorbed from the tissues mainly by direct entrance into the blood vessels, or into the lymphatics, or both. Horse serum given dogs subcutaneously appears in the thoracic duct lymph within 40 minutes, but is not detectable in the circulating blood for several hours. Inflammation retards the absorption of diffusible substances less than nondiffusible ones; in fact, there is actually speedier absorption of diffusible carbohydrates and dyes, when they have been injected intracutaneously, from an inflammatory site than from a normal one.

Immediately after the injection of an irritant into a rabbit's skin there is a temporary great increase in the resistance of the vessel walls, and this is soon followed by a decrease in resistance. When the irritant injected is turpentine or streptococcic material, the resistance falls to normal within 2 to 9 days. With staphylococcic or pneumococcic material, resistance is raised above normal for a few days. It remains above normal for a week or more with tuberculin. In allergic inflammation, the preliminary period of resistance is sometimes diminished, and fragility hastens in onset (Zander: JExpM 66: 637, 1937).

The Shwartzman Phenomenon is a hemorrhagic and necrotizing inflammatory response which appears promptly after the intravenous injection of a bacterial filtrate in a site which 24 hours previously was injected intracutaneously with that bacterial filtrate (Shwartzman: *Phenomenon of Local Tissue Reactivity*, Hoeber, 1937). This type of reaction may perhaps underlie the relationship of focal infection with certain disease processes.

Such inflammation was described by Stenn (APath 26: 44, 1938). Swelling at the site leads to necrosis. There are seen polymorphonuclear cells, distention of the tissues with serous and fibrinous fluid, necrotic nuclei and swollen nuclei of fibroblasts, red blood cells in the interfibrillar spaces, and hyaline thrombi in the capillaries, small veins and lymphatics surrounding the necrotic focus. Polymorphonuclear and monocytic leucocytes encircle these channels and penetrate the walls. In the periadventitial tissue the cellular infiltrate resembles granuloma. Increased capillary permeability allows the outpouring of fibrinogen, the deposition of fibrin, and the thrombotic local fixation of foreign material.

**Immunology.**—The skin is *an important organ from the standpoint of immunity*. The breadth of its function is indicated by the fact that a great variety of antigenic substances inoculated intracutaneously evoke responses which are characteristic and useful for diagnostic purposes. Among such tests are those for tuberculosis, chancroid, Brucella infection, trichophytosis, moniliasis, ecchinococcosis, and venereal lymphogranuloma. *Percutaneous immunization is possible.* Intracutaneous immunization requires comparatively little antigen.

**Specifically Altered Reactivity (Allergy)** of the skin is closely interrelated with immunity. From a broad standpoint an allergic reaction is an ineffectual and distorted immunologic one. Allergic reactions comprise not only specifically acquired hyper reactivity (hyperergy) but also specifically acquired hyporeactivity (hypoergy) and specifically acquired immunity (anergy). Excessive reactivity of the skin varies as to degree. In a given skin, reactivity may fluctuate with nervous, emotional or physiologic activity. An allergic response depends on contact of the noxious

substance (allergen) with the susceptible skin, immediately in the form of solid liquid dust, or gas or mediately by way of the blood. (Sulzberger et al. J 104 1489 1935 YBD 1943 p 7 1944 p 7; 1945 p 7)

**Alteration of Reactivity** does not denot allergy unless the alteration is pecific A skin irritated by a cau tic, for example manifest sen itivity to mercuric chloride but not specific hypersensitivity a skin manifesting contact dermatitis, whatever the cause usuall manifests excessive irritability to soap, and its erythema is in tensified by warmth, but these are not allergic reactions.

Von Pirquet and Schick (Die Serum Krankheiten, Leipzig 1905) found that an animal once injected with a foreign serum react to a second i jection in a dif fere t manner They howed that, in order to obtain this changed reaction time m st elapse between the first and second injections. They noted that this period *of from 8 to 12 days correspo d to th i cubation period of many infection dis-orders.* For altered reactivity they suggested the term allergy One dose of horse serum provokes hypersensiti ity in the guinea pig but repeated tol rated doses i luce immunity reported W l (JMRes 1 40 1913) and the serum of the im m nized animal will induce hypersen itivity in a norm l one Weil i dicated thus that the same antibodies are p ese t in allergy a in immunity but in the former their locat on is predominately in the cells, and in the latter in the serum. The immunized a imal is potentially anaphyla ti bi cells possessing anchored immune bodies but he is protected by immune bodies in his circulation. Allergic reaction apparently is due to rea tion between specif antibodies in cell with the introduced antigen. In immun ty on the other hand, antibodies present in the serum neu-tralize introduced antigen a d so protect bod cells.

It is believed that as a result of antigen antibody reaction tored up vasodilator substances are set free f om th fixed t sue cells and these freed, histamine-like substances a e the mmediat ause of the typical allergic reaction (Dale and Laidlaw JPhys 5. 335 1910) It may be that histamine is actually the noxa so released, for histamin se said t d minal h allergic reactivity and injections of histam e may induce refra tori ess t h stamine and diminution (but not dis-appearance) of allergic rea t ity (Edit. J 115 1023, 1940) Benadryl relieves serum sickness (Peterson and B hop J 133 1— 194 ) and antihistamine drugs are ffectively palliat ve i urt caria hay f er and asthma, presumably by virtue *of thei abil ty to null fy h tam ne*

Allergy t food ha been kn wn a cause of abdominal pa n and gastroin-testinal symptoms, urticaria, d rmat t migraine a d bronchial a thma. It affect adult as well as children. It i not a common a fact r in dermatoses as most persons imagi e

**The Arthus Phenomenon** hara t rized b the provocation of progressive infiltration induration, edem nd awept gangrene in a site repeatedly i jected with a foreign prote n. Su h a ph lactic ga gre ha foll wed the repetit on of injections f t sera i t huma bei gs (Tumpeer et l. J 96 1372, 1931; Irish and Reynold J 100 490 1933)

**Sensitization of Contact Type** (without circulating antibodies) to simple chemical substances may be induced by injection of conjugates of the simple substance with certain proteins, such as red blood cell stroma (Landsteiner and Chase JExpM 73 431 1941) Conjugation with *staphylococcus toxin may render autogenous proteins, such as rabbit skin,* antigenic to the homologous or even the same animal (Hecht et al. J ExpM 78 59 1943)

If skin is c rcumvallated by incision and the island so produced then sensitized by dinitrochlorobenzol, the island may be sensitized while the remainder of the skin remains nonallergic. In control sensitization of a spot produces sensitization of the whole. So skin contact sensitization seems t spread in the cells, not by way of the blood (Schreiber and Muller DWehn 107: 1393 1935)

Haxthausen (YBD 1945 p. 141) transplanted skin sensitized to dinitrochloro-benzene from one identical twin to an ther replaci g the donor area with non-sensitized skin from the normal tw n. Three weeks after transplantation previously normal skin growing in the sensitized twi had become sensiti e, and the previously sensitized skin now attached to the normal twin was not react ve The capacity to react

did not move with the full thickness transplant, but its presence or absence was determined evidently by influences outside the transplant. See Rostenberg (ADS 56: 222, 1947)

Correlation of susceptibility to allergy and emotional and psychiatric aspects of the individual has received consideration, and it is thought by some that the "allergic personality" may exist (Stokes and Beerman PsychosomM 2 438 1940)

Sensitization may be provoked by the most diverse substances, as study of the articles on urticaria and contact dermatitis shows.

Hyposensitization is a state of partial protection which is induced by small, repeated doses of an allergen. "Hardening" occurs in perhaps 90 per cent of industrial employees who handle irritating chemicals (such as TNT), an ability to withstand further contact without irritation, a fact which Schwartz taught skeptical dermatologists. Abstinence from contact with the sensitizer may be followed in a few months by loss of this immunity. The case usually seen by the dermatologist is the one who is unable to develop hardening, Schwartz pointed out.

The therapeutic establishment of an antianaphylactic state is not often satisfactory in dermatology. It is better to discover the offending material, if possible, and to segregate the patient from it.

Histologic changes are correlated with immuno-allergic processes. When local reaction rapidly destroys, attenuates, or otherwise renders innocuous microorganisms or their products, tuberculoid structure usually is found (Jadassohn-Lewandowsky "law"). Tuberculoid structure is not seen as a response to drug allergy.

Configuration of lesions grossly is also frequently correlated with immuno-allergic processes. When a zone of absolute or relative specific resistance develops peripherally, the local process may assume a corymbiform shape for satellite lesions are impeded in their growth. Central healing results in annular shaping, for the healed zone manifests increased immunity while the centrifugally spreading margin represents immunologic activity.

While disease processes as witnessed are often explained by immuno-allergic theory, explanation of the explanation leaves a good deal to be desired. Compare these arguments: (1) annular shape results from development of immunity in the central part of the lesion so that the central part heals and (2) the central part has healed, so that immunity may be assumed to have developed there. Some investigators appear to see from within outward.

SKIN TESTS are immunologic procedures designed to ascertain the skin's capacity to react. "They can be so standardized as to show whether cutaneous tissues have acquired some alteration in their capacity to react to certain agents. ... They are never the sole diagnostic method, and positive reaction is never proof of causal role, while negative reaction never completely exonerates an agent," wrote Sulzberger and Baer (YBD 1943, p. 7). Performance, interpretation, and exhaustive tabulations (diseases, concentrations, and precautions) of skin testing are given in this reference. Practical application in occupational disease, along with warning that unnecessary or unwise testing may cause severe reaction, is discussed by Downing (ADS 48: 614, 1943). Skin testing with a food extract killed a patient of Swinsford (JAllergy 17: 4, 1946).

Tests for sensitivity are of the contact, scratch, and intracutaneous types. The intracutaneous test requires the least of the irritant material to cause reaction. The contact, or patch, method of testing is suited for determining susceptibility to external irritants. These tests serve to reproduce a disease in miniature under controlled conditions. Passively transferable elements occur in the blood

idiosyncratic individuals (Prausnitz and Küstner: Zentralbl. f. Bakt. 86: 160, 1921). In some instances, allergens affecting the skin are absorbed through the colon or via the respiratory route. In general, allergens that damage the epidermis are fat soluble and produce vesiculation, while those to which the dermis reacts are water soluble and evoke wheals.

CLASSIFICATION OF ALLERGIC PHENOMENA.—Sulzberger and Goodman (JAMA 143: 1936) defined allergy as an altered state of reactivity altered by a first contact and made manifest by subsequent specific contacts. The term allergy must therefore include acquired hypersensitivity, hyposensitivity and absence of sensitivity, all probably due to closely related mechanisms.

I. Anaphylaxis—occurs in laboratory animals, is specific, is linked with particular phenomena, is associated with antibodies which occur with (and may be identical with) precipitins.

II. Human Allergy—atopic and nonatopic:

A. ATOPIC:

a. The symptoms are explicable by increased capillary permeability and smooth muscle spasm.

b. Family and personal history often include asthma, hay fever, atopic dermatitis.

c. Eosinophilia in smears, transudates, secretion.

d. Positive scratch or intracutaneous skin tests with wheal and flare response; patch tests usually negative.

e. The presence of circulating antibodies, which are transferable (Prausnitz-Küstner).

f. Allergens are atopens and may be pollens or other plant emanations, or emanations from animals or insects, spores, dust and powders, food, clothing, cosmetics, serum, vaccines, parasites, drugs, or other substances, usually proteins.

B. NONATOPIC

1. *Contact Allergy* (eczematous or epidermal allergy)

a. May occur in any individual after adequate exposure;

b. Is manifest after a time interval (incubation period) following the sensitizing contact with or without repeated exposure;

Lesion, caused by unknown mechanism, is epidermal and eczematous with papules and vesicles, microscopically spongiosis (intracellular edema, necrosis and acantholysis).

d. No wheal reaction, no circulating transferable antibodies, no family history of atopy.

Cause can be identified by eczematous reaction to patch test (and by flare of preexisting lesion in many instances).

f. Relief on avoiding irritant; recurrence or exacerbation on exposure.

g. Allergens are not antigens (evoke no antibodies); they are simple chemical substances, plant oils, product of fungi or bacteria, rarely protein.

*Drug Allergy*

a. Provoked by drug ingested, injected, inhaled, absorbed or in contact [we prefer to place contact dermatitis caused by medicinal chemicals in the same class with other contact allergies].

b. No circulating antibodies.

Urticarial reaction to scratch or intracutaneous test in rare urticarial drug eruptions; patch test reproducing eczematous or vegetating lesion in that type of drug eruption; eczematous reaction to patch test in medicinal contact dermatitis.

d. Relief upon avoidance; reproduction of dermatosis upon administration of the offending drug.

e. Caused by drug allergens, which are not antigens or atopens.

2. *Allergy of Infection*

a. Nonatopic allergy brought about by infection or by adequate contact with living agents, characterized by specifically altered reaction to them or their products;

b. Reaction may be hyperergic, hypoergic or anergic;

c. Recognized by proof of infection, by altered reaction to reinfection, by skin tests and other tests (with the offending agents or their products or immunologically related substances), the intracutaneous reactions usually being of 48 hour tuberculin type;

d. Relief by the individual's mastering of the infection, by eradication of focus, by specific hyposensitization (immunization) procedures
e. Causal agents often antigens may be bacteria, fungi, viruses, protozoa, etc.

4. *Foreign Protein Allergy* (Noninfections):
   a. Recognized by immediate and delayed reactions of local, general, or systemic character of the form of anaphylactoid shock, *urticaria*, *toxic dermatoses*, serum sickness, following exposure to such substances as foods, inhalants, serums, animal products.

5. *Physical Allergy*
   a. Not strictly according to definition, being not caused by a substance
   b. May act by producing substances in the body which in turn produce manifest reactions;
   c. Reaction is evoked by heat, cold, light, mechanical irritation, in amount and manner usually harmless to normal individuals
   d. Recognized by elimination of other forms of allergy, relief on avoidance, production of symptoms on exposure;
   e. Hyposensitization may be possible by measures designed to increase tolerance.

Forms of Allergic Reaction.—Sulzberger and Goodman continued with an epitome of the forms of allergic reaction: Allergic reactions can occur in all organs, in any organ, in any part of any organ, and in any system. Atopic reactions favor the mucous membranes of the nose, the conjunctivae, the bronchioles, and the vascular apparatus of the superficial cutis. The reactions of the contact form of allergy are located primarily in the epidermis. The skin is frequently implicated in many different forms of allergy, but no organ is immune. The commoner forms of allergic response include

## A. Localized Reactions

Hematologic System: bone marrow, lymphatic system, perhaps the blood cells themselves: agranulocytosis, thrombocytopenic purpura, etc., eosinophilia.

Eyes: especially iris, conjunctiva, lens, iritis; vernal catarrh, etc.; cataract in atopic dermatitis.

Nose and Sinuses: rhinitis, acute and chronic sinusitis, polyps.

Bronchi and Lungs: asthma; other acute and chronic infectious and noninfectious processes.

Skin: contact dermatitis, urticaria and angioneurotic edema, atopic dermatitis, miscellaneous dermatologic manifestations, such as generalized or localized erythemas, nodose and multiform erythemas, drug eruptions (acneform, furunculoid, fixed, purpuric, etc.), infectious exanthemas (syphilis, leprosy, exanthemas of childhood, etc.)

Gastrointestinal Tract: various types of acute or chronic, spastic, or inflammatory reaction.

Liver: acute yellow atrophy, arsphenamine jaundice, etc.

Genitourinary Tract: cystitis (?), nephritis (?)

Joints: arthritis, intermittent hydrarthrosis.

Central Nervous System: migraine, epileptiform seizures, asthenia, psychic disturbances (especially in children), neuralgia, transient paralysis and nerve dysfunction (?), and perhaps some organic diseases, such as multiple sclerosis.

Cardiovascular System: hypertension (?), hypotension (the rule), cardiac irregularities, tachycardias, extrasystoles, bradycardias, precordial pain. Buerger's disease (?), migratory phlebitis (?), periarteritis nodosa (?)

## B. Generalized Reactions

Allergic Shock: subnormal temperature, low pulse, lowered blood pressure, prolonged coagulation time, increased N P N, decreased blood chlorides, decreased blood calcium and phosphorus, decreased sugar tolerance, leucopenia.

# SYMPTOMATOLOGY AND PATHOLOGY

Dermatologists are not strict rhetoricians in the differentiation of symptom and sign. Dermatoses are brought to them by their patients because of itching more commonly than for any other single complaint. Itching, burning, tension, dryness, cracking, crawling, tingling, soreness, pain, numbness are words used by the sufferer. He may feel a bump or roughness or describe his sores or blisters, or complain of an sightliness. He may be heeding the excellent advice nowadays well publicized, to attend to a small matter even though asymptomatic because its consequences lie not within his knowledge.

Objectively external manifestations in cutaneous medicine are composite pictures resulting from the conjoint development of various elementary lesions. These essential primary eruptive elements are relatively few and simple. As a result of the continued action of a pathologic process, secondary infection or trauma, primary lesions may undergo various modifications, and so be transformed into consecutive or secondary lesions.

The following definitions of gross and microscopic lesions afford a basic vocabulary for description of what is to be seen. But they are not sufficient for the dermatologist is obliged to add numerous adjectives, concerned generally with color, texture, distribution, temperature and even odor in order to describe with some accuracy and completeness. His finger tips help a dermatologist greatly and his nose not a little.

**Gross Lesions.**—Each has an underlying histologic basis, and the student must constantly strive to interpret from visible processes their microscopic make up. The microscope is only an adjunct to the eye, it does not introduce a new world. Any lesion is a manifestation possessing three dimensions in space and a fourth in time and yet another in the psychologic and sociologic relationships of an individual.

### Primary Gross Lesions

1. **Macules** are circumscribed discolorations of the skin which are neither elevated nor depressed.
2. **Papules** are small, variously shaped circumscribed, solid elevations.
3. **Wheals** are rounded, elongated, or irregularly shaped, edematous transitory elevations of which hives are typical examples.
4. **Nodules** are circumscribed, solid masses which may lie above, level with, or beneath the surface. Tubercles are nodules of bean to pea size, firm, and deeply seated. Tumors are soft or firm, variously shaped lumps of relatively large size.
5. **Vesicles** are circumscribed pinpoint to pea sized elevations containing free serous fluid. Blebs, or bullae are vesicles of large size. The burrows of scabies are linear mite made vesicles, overlying secondary inflammation.
6. **Pustules** are circumscribed elevations containing free purulent fluid.
7. **Telangiectases** are tiny red linear lesions due to the presence of dilated capillaries.

### Secondary Gross Lesions

1. **Excoriations** are discontinuities of the skin, usually superficial in character and traumatic in origin.
2. **Fissures** are linear breaches of continuity generally sharply defined with abrupt walls, and inflamed bases.
3. **Scales** are dry or greasy laminated masses of superabundant epidermis. They range in size from minute furfuraceous fragments to large sheets of horny material.

4. Crusts are masses of dried exudate.

5. Ulcers are irregularly sized and shaped excavations of the integument due to injury or disease. The majority involve the connective tissue and in healing generally produce scars.

6. Scars, or Cicatrices, are connecti e tissue new formations which replace loss in substance in the fibrous layer of the skin.

**Microscopic Lesions** are the basic morphologic changes upon which rest the gross evidences of disturbance. They may be cellular intercellular humoral, or mixed. Inflammation is discussed as a physiologic process on p 26 Histologic descriptions of diseases are found throughout the text.

### Changes in the Epidermis

1. **Hyperkeratosis** is hypertrophy of the horny layer as in calluses. Nuclei are not visible in the keratin mass.

2. **Parakeratosis** is retention of nuclei in the cells of the horny layer due to defective keratinization.

3 **Acanthosis** is thickening of the stratum germinativum due to increased mitosis in the rete cells.

4. **Inclusion bodies** are intracellular bodies, such as are seen in Darier s disease, highly anaplastic carcinomas, and virus diseases, such as herpes, molluscum contagiosum, and variola.

5. **Atrophy** consists in general thinning of the epidermis with diminution in the accessory epidermal structures and flattening of the papillae. It is usually due to defective nutrition from the corium, or to stretching over an enlarging dermal mass.

6. **Edema.** Intercellular edema, or spongiosis, is shown by widening of inter cellular spaces. If the severity is such as to rupture the intercellular bridges, the result is an intraepidermal vesicle. Intracellular edema takes several forms. In reticulierende collaquation, vacuoles develop in the protoplasm of several cells, the nuclei degenerate, the cells swell to bursting, and multilocular vesicles are formed. In ballonierte degeneration, young epithelial cells balloon up and become loosened one from another so forming a vesicle. In alteration cavitaire, the protoplasm becomes homogeneous and stainless, and perinuclear edema appears which may increase till the cell ruptures, a third method of intraepidermal vesicle formation.

7 **Neoplastic proliferation** occurs from the epidermis (basal-cell and squamous-cell carcinoma) and from the epithelium of accessory structures (epithelioma adenoides cysticum) Malignancy is indicated by profusion of mitoses, metaplasia of the cells, invasion beyond a basal membrane and abnormal position of active epithelium.

8. **Pseudoepitheliomatous hyperplasia** exists when the normal epidermis is notably hyperabundant, as it may be in response to granulomatous inflammation of dermal papillae or t the edges of hronic ulcers.

### Changes in the Dermis

1. **Fibrous tissue** may be hypertrophic (keloid elephantiasis) or trophic (old irradiation scars, senility) It may undergo colloid hange, as in hyalinization of old scars or mucoid change as in x-ray dermatitis. Amyloid deposits may occur about the capillary loops. Lipoids of various kinds may be deposited intracellularly e intercellularly or both. In rare instances calcification is found. Degenerate collagenous tissue which stains like normal elastic tissue is called collastin. Burns, caustics, powerfully toxic substances, and vascular occlusion are causes of necrosis.

— **Elastic tissue** may be overabundant as in cutis hyperelastica, or defective, as in epidermolysis bullosa. Elastic fibers that become thick, swollen broken up and bnormal in staining properties form what is called collacin.

3. **Infiltrative changes.** These are usually perivascular and perifollicular Cellular collections consist of various proportions of polymorphonuclear leucocytes, lymphocytes, mast cells, plasma cells, and cells of reticulo-endothelial origin includ ing giant cells. Histiocytes are cells capable f ingesti g foreign substances. The infiltration may be circumscribed, or limited to relationship with certain struct res; or it may form a massive cell filtrate without reference to vessel or glands. W th inflammatory infiltration are associated fibroblastic nd endoth lial proliferation. Acut processes are characterized by numbers of polymorphonuclea leucocytes; more chronic ones have higher proportions of lymphocytes, eosinophiles, and plasma cells.

4. Vascular changes consist of vasodilation as in mild sunburn, edema, wherein fibers are further separated than is normal and may take a foggy stain; hemorrhage by rupture as in trauma or by diapedesis as in purpura, inflammation; and occlusion, partial or complete as in diabetic gangrene. Necrosis occurs in new growths which outrun their vascular supply as in gumma or caseating tubercles.

5. Pigment occurs in chronic inflammatory conditions as an oversupply of melanin. It occurs abnormally as hemosiderin after hemorrhage into the skin. It is produced abnormally in large quantity as melanin in both benign and malignant neoplasms. Pigment of extrinsic origin occurs in tattoo.

6. Neoplastic change in the corium may affect any structural element there present. Hemangioma, lymphangioma, fibroma, neuroma, myoma, even osteoma, are found along with sarcoma of various kinds, primary or metastatic.

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# ETIOLOGY

In the skin the changes that take place as a result of disease follow the same laws that apply to changes in other parts of the body Damage may be sustained directly or indirectly Indirect damage may be mediated by the blood vascular lymph vascular or nervous system. Many disorders of the skin are secondary to some derangement of the internal economy Others originate in the skin itself and confine their action to this organ alone. The skin is exposed to injurious agencies as other organs are not. Combinations of factors are frequently at work in any given patient, so that a dermatologist must daily unravel problems which necessitate a multiplicity of simultaneous diagnoses, a multiplicity astonishing to monodiagnostic purists. For example an age-sex-occupation predisposition in combination with a trauma medicinal parasite excitation may explain a secondarily infected, medicinally irritated hangnail on the finger of a stenographer whose digits would not have been rough if she did not scrub off carbon, and who developed sensitivity to the phenol-sulfonamide component of nail lacquer when she scratched her pruritic disease, and who got a generalized, severe eruption when the infection was treated with a sulfonamide by mouth.

**Predisposing Causes.**—Age.—Some diseases of the skin usually develop only at certain periods of life, while others may appear at any time Ichthyosis, angioma epidermolysis bullosa, and congenital syphilis appear in infancy Children are particularly susceptible to the parasitic diseases, such as impetigo tinea capitis, and favus. Acne vulgaris and psoriasis usually start in early adult life. Pruritus and carcinoma are diseases of an older age.

Sex is a factor in the etiology of many cutaneous disorders, not only hormones but also habits being concerned.

Race and Nationality —The proclivity of the Negro to keloid for example is well known (Lewis PIMChi 17 112, 1948)

Heredity —Familial incidence is a feature of some dermatoses as in ectodermal dysplasia, keratosis palmaris et plantaris and epithelioma adenoides cysticum. Most persons who develop squamous cancer of the exposed skin have inherited their susceptible blond and sun-sensitive skins. Syphilitic infection may be acquired by the fetus from its mother during gestation. An hereditary bent toward sensitization of the urticaria eczema-asthma type is recognized

Seasons.—Prickly heat pruritus aestivalis, and the superficial staphylococcic infections are usually diseases of the summer months. Ichthyosis and psoriasis are generally more troublesome in winter Diseases of plant or animal origin, such as ivy poisoning ragweed dermatitis harvest mite and spider bites, manifest seasonal frequency of occurrence for obvious reasons.

Occupation —Numerous irritants are used in both household work and trades, and so frequently do these various substances give rise to dermatitis that occupation dermatoses (p 85) comprise an important class of dermatoses, which are of medicolegal importance.

Coexisting Organic and Constitutional Diseases.—Sometimes the development of a cutaneous disorder largely depends on the coexistence of an organic or constitutional disease. Tuberculosis, scrofuloderma, and the tuberculids are frequently closely associated, as might be expected. The relationship of diabetes mellitus to xanthoma diabeticorum and to moniliasis, pruritus, and staphylococcic parasitism is a matter of common observation. Cutaneous manifestations occur in the majority of systemic diseases. See Wiener *Skin Manifestations of Internal Disorders* Mosby 1947

Focal Infections.—A persistent nest of pathogenic microorganisms may reside in dead or abscessed teeth, pyorrheic gums, tonsils or tonsil stubs, paranasal sinuses, vagina, pelvic organs, prostate, bladder or rarely appendix or gall bladder. Occasionally escaping from the focus, these may provoke or abet or complicate cutaneous disease. A skin which has been chemically irritated may be vulnerable to bacteria of the oral flora which were previously unable to invade the skin. (See p. 708.) In focal infection in the mouth streptococci are the usual agents. Monilia, too, occur in focal infections, particularly of the vagina or nails, and cause trouble when opportunity avails. See Edit. (J 113 111 1947)

Psychologic and Psychiatric factors are significant and are receiving increasing recognition. Because of personality make-up some people wash too much, scratch too much, sweat too much, misinterpret or overemphasize abnormalities, or perform unwholesome acts. A dermatologist should develop his amateur psychiatric ability. One must possess inquisitiveness regarding and wide knowledge of how people think, feel, respond, live, and do things if one would interpret skin diseases, understand them and sometimes cure them. See Obermayer (J 122 862, 1943) Hodgson (BJD 57 125 1945) Klaber et al (BJD 59 1 6 13 1947) also p. 468

**Exciting Causes** in diseases of the skin may be internal (constitutional), external (local), or both. Often it is difficult or impossible to locate the exact etiologic factor.

Trauma.—Injury limited to the epidermis heals without scar by the mitotic outgrowth of cells in sheets from near by epithelium and the new skin cannot be differentiated from the old. When fibrous tissue is lost or more is produced because of gaping of the wound edges, a scar is inevitable. Trauma introduces microorganisms into a position in which their activity may have deleterious effects. Trauma produces temporary dilation of capillaries and so erythema or sufficient damage of vessel walls to allow transudation and whealing or even vascular rupture with resultant petechiae and ecchymoses.

Temperature.—Burns and congelations are discussed on pp. 65 ff.

Light has profound effects on the skin. Infrared rays are absorbed by the superficial layers, while the short red rays penetrate and can heat tissues at a depth of 0.5 cm to a temperature higher than the surface itself. Ultraviolet rays hardly penetrate the epidermis. The biologically active region of the spectrum is from 3 130 A.U. to 2 900 A.U. Ultraviolet rays are absorbed by the cells and cause necrosis by specific action on the cytoplasm. Pigmentation and the ability to produce pigment are factors differing in individuals. Light sensitivity may be pathologic (p. 89). The effects of irradiation of an area painted with oil of bergamot are much enhanced (p. 89). Several photodynamic sensitizers are known, the presence of which renders the tissues vastly more susceptible among

these are eosin, acridine, and hematoporphyrin. The activation of skin cholesterol by ultraviolet light results in the production of vitamin D

RADIATION from radium and x ray is discussed under roentgen therapy (p 55) and x ray dermatitis (p 72)

CHEMICAL SUBSTANCES affecting the skin from without are classified with difficulty They range from those which affect every skin, such as undiluted nitric acid to those which affect only a few skins, such as turpentine or any other of the host of substances that provoke dermatitis venenata (p 75) While concentration and duration of contact have much to do with the results of contact, individual allergic idiosyncrasy is an equally important factor Often the first contact evokes no apparent response, but later contacts with the altered and susceptible skin provoke violent reaction. This is true of such substances as the poison of poison ivy; but why this is so remains a problem.

TOXIC SUBSTANCES of chemical nature may affect the skin following ingestion or injection. The manner of action is by no means understood and individual sensitivity is highly variable. (See Dermatitis medicamentosa, p 100 )

PARASITES.—The skin is normally host to many kinds of saprophytic organisms. Some of these waver between innocence and harmfulness so that circumstances favorable to their growth result in the development of symptoms. Moisture, warmth, and darkness are the principal of these and so it is that the stout woman in the summertime complains of irritation beneath her pendulous breasts. (See Skin flora, p 24 and specific parasitic dermatoses.)

NERVOUS CAUSES.—It is probable that the nervous system is a contributory factor in the etiology of a number of dermatoses (see psychologic factors, p 36, and psychosomatic aspects, p. 468) In some of these, such as hyperidrosis, glossy skin and pruritus, a direct relationship can be traced, while in others such as neurodermatitis, alopecia areata and scleroderma, the evidence is hypothetical. There is a tendency for physicians to attribute dermatoses of unknown origin to nervous influences, just as the laity attribute troubles to acid in the system. See Lewis and Cormia (NYSJM 47 1889 1947) and Brunner (ADS 57 374, 1948)

METABOLIC DERMATOSES include the skin changes in dietary and endocrine disorders. Disturbances of metabolism of several classes of chemicals may cause cutaneous manifestations. See pp 384 ff

NEOPLASTIC DISEASE.—Studies of the cutaneous effects of sunlight, x ray and tar and its derivatives offer as hopeful a prospect as any field of inquiry into the nature of neoplasia In the skin the earliest processes can be seen and followed.

ALTERED REACTIVITY (ALLERGY) —See p 27

# DIAGNOSIS

Confronted by an individual with a skin disease the student has a problem to solve. A routine of complete examination is indispensable. Accuracy and patience are essential. Dermatologic diagnosis is eminently based on objective evidence and in general it is wise to look first and ask questions after. Gentleness and tact should be exercised especially in dealing with women. Dispensary patients should receive the same consideration as that extended to private patients. Particularly in cases of puzzling nature the entirety of the patient's skin must be examined. Diagnostic error is more likely to be due to incompleteness and carelessness than to ignorance.

At first glance one notes the apparent age, sex, and general condition as regards nutrition, hygiene and malaise. One looks at all of the eruption, removing and replacing clothes if need be and notes specifically the distribution of the lesions and evidences of grouping, then the primary and secondary gross lesions. Evidence of pruritus is visible as linear scarification and absence of tops of lesions, and in chronic cases the nails are worn and polished. The type of exudate is seen to be serous, glairy, serosanguineous or purulent. Crusts may need to be removed (benzine is useful) in order to see the bases of ulcers. Scales may be lifted to determine their adherence, noting the presence or absence of uncovered bleeding points. The lesions are palpated and the sensations of resistance, edema, induration, infiltration or cystic structure are felt. Important is examination of the lesion pressed under a watch crystal (diascopy) which discloses the color unmasked by the presence of capillary blood. Apple butter nodules of tuberculous disease are rendered evident, redness of extravasated blood as in purpura does not vanish under pressure while that due to simple hyperemia does. The oral mucosa is examined and the condition of teeth, gums, and tonsils noted. The general and regional lymphatics *should be palpated.*

At this stage the observer has sufficient data to form a fair idea of the kind of trouble at hand. He has been asking himself whether the complaint is internal or external in origin and whether it is chemical, parasitic or neoplastic in cause. But after examination he should know whether the lesion is hyperemic, inflammatory or hemorrhagic, whether it primarily affects the skin or skin appendages, whether it is an irritation, infection, symptom of general disease or new growth, and he should be able to make a canny surmise as to its duration and symptoms. Cutaneous manifestations of systemic disease must be recognized (Montgomery, Minn.M 22 451 1939).

*He may now add to his data pertinent subjective information* as to occupation and habits, the duration and sequence of the eruption, and the complaints of itching, pain or unsightliness. Further questioning of the patient may be desirable or necessary regarding the functions of the various bodily systems, including the endocrine and the feelings of the patient and his interrelationships of emotional and sociologic nature with other people. These facts are important in formulating treatment, for one must treat the patient, not simply his disease.

Scrapings from the lesions digested in 10 per cent potassium hydroxide are examined microscopically if fungus infection is to be tested. Exudate may be examined for "sulfur granules" of ray fungus, acid fast bacilli, streptococci, spirochetes. Cultural methods are needed for accurate identification of the mycoses. Biopsy furnishes the histopathologic picture (Rhoden: ADS 47: 580 1943) Various stains may be applied.

If indicated a general medical examination must be performed, and while few dermatologists excel with the stethoscope they should know how to palpate a spleen. The blood picture cell counts, hemoglobin, and sedimentation rate while requisite to thoroughness in a hospital, are not routinely done in private practice; but leucemia or agranulocytic angina is hard to diagnose by guesswork. The value of the Kolmer Wassermann and related tests is evident. Chemical examination of the blood has its place X ray examinations of teeth and sinuses are required in running down focal infections; roentgenograms are indicated of tumors attached to bone and of vertebrae, long bones, and skull, in search of metastases. Spinal fluid must be examined in syphilitic patients. The basal metabolic rate may be informative. (Lemeravski: AmdeD 10: 177 1939.)

Dermatoscopy by slit lamp or corneal microscope reveals the horny layer and epidermal portions of sweat gland ducts and hai follicles, the pigment, and the most superficial blood vessels. Suitable apparatus is expensive and seldom used. (Michael ADS 8 603 1923.)

Wood's light has considerable diagnostic utility especially in the treatment of tinea capitis (p. 307) Fluorescence diagnosis was discussed by Costello and Luttenberger (NYSJM 44 1778, 1944) and Rosebeue (RhodeIsMJ 29: 34, 1946) If fluorescein is injected intravenously and the skin lesio examined with Wood's light several varieties of response may be observed (Herrmann and Kanof JIn D 8: 4-1, 1947) In lesions with increased blood flow hyperfluorescence appears rapidly before the dye is visible in normal skin and disappears rapidly while the normal skin is still fluorescent. Inhibition of fluid exchange between circulatory system and vesicle contents results in delayed appearance and persistence of brightness in the vesicles of herpes. In passive congestion and venous stasis, the lesions remain dark, as in varicosity telangiectasis, and rosacea. Psoriatic papules are dark surrounded by hyperfluorescent halos. In lichen planus and lupus erythematosus, one finds spotty hyperfluorescence in otherwise dark lesions. Bright lesions may be expected t heal rapidly while dark lesions tend to respond poorly

Diagnosis aims at establishing etiology as well as classification. Patch tests and intracutaneous sensitivity tests are further methods of attack. The inquisitiveness and ingenuity of a Sherlock Holmes are required in the elucidation of many problems, and despite the most modern apparatus and methods of attack, one's ignorance as frequently confronts him as his learning. Dermatology is an orchard heavy with fruit awaiting the investigator's grasp

## REGIONAL DISTRIBUTION OF COMMON DERMATOSES

**Anal Region.**—Pruritus, condyloma, hemorrhoids, tinea, intertrigo, contact dermatitis (soap and medicines) folliculitis, oxyuriasis.

**Bearded Region.**—Impetigo, dermatitis venenata, sycosis, tinea barbae, alopecia areata, sinus tract of dental origin

**Breasts.**—Dermatitis venenata, infection eczematoid dermatitis, carcinoma Paget's disease scabies, intertrigo.

**Chest and Shoulders.**—Seborrhea, acne, syphilids, tinea versicolor, seborrheic keratoses, scabies, psoriasis, pediculosis, drug eruptions, the acute exanthems.

**Crural and Axillary Regions.**—Tinea, seborrheic dermatitis, intertrigo, dermatitis venenata, streptococcic dermatitis, scabies, furunculosis, hidradenitis, infectious eczematoid dermatitis.

**Ears.**—Seborrheic dermatitis, streptococcic dermatitis, otomycosis keratosis, carcinoma, frostbite painful nodule.

**Eyelids.**—Dermatitis venenata, xanthoma palpebrarum, molluscum contagiosum, keratoses stye chalazion, a itaminosis B, seborrheic dermatitis (Haren ADS 49 253, 1944 Ormsby AmJOphth 26 830 1943.)

**Face.**—Freckles, chloasma, vitiligo seborrheic dermatitis, dermatitis venenata, impetigo, erysipelas, acne rosacea, milium, rhinophyma, syphilids, lupus erythematosus,

erythema multiforme lupus vulgari nevu angioma, seborrheic keratosis carcinoma, herpes implex, molluscum contagiosum. (Thorek: *The Face in Health and Disease* F A. Davi 1916.)

**Forearms and Legs.**—Infectious eczematoid dermatitis, dermatitis venenata, ecthyma, urticaria lichen planus psoria is, erythema multiforme erythema nodosum, purpura, ichthyosi keratosis pilaris, syphilid atopic dermatitis (flexures) lichen simplex, stasis dermatiti , purpura.

**Genital Region.**—I ro tus, scabies, pediculosis, seborrheic dermatitis, herpes simplex, chancre chancroid lymphogranuloma venereum, syphilids lichen planu car cinoma, dermatitis venenata, kraurosis, lichen sclerosus, tinea.

**Hands and Feet.**—Vitiligo, tinea dermatophytid, dermatitis venenata, streptococcic dermatitis scabies, hyperidrosis, pompholyx palmar and plantar keratoses, infectious eczematoid dermatiti erythema multiforme s philis dermatitis repens, verruca, carcinoma (hand ) x ray dermatitis. (Madden, Nomland Caro, Montgomery Kulchar: J 1 1; 743 ff 1911 feet; Lane JMichMS 39; 540 1940 hands.)

**Lips.**—Herpes simplex, leucoplakia, carcinoma, chancre mucous patches, cheilitis exfoliativa cheiliti glandularis postematosa, Fordyce s disease urticaria, retention cysts contact stomatitis, lupu erythematosus, fissure

**Neck.**—Lichen simple seborrheic dermatiti dermatitis venenata (wool fur cosmetic), cutaneous tags

**Scalp.**—Seborrheic dermatitis, dermat tis venenata, psoriasis, tinea (children only) lupus erythematosus pediculosi capitis infectious eczematoid dermatitis, premature alopecia, al pecia areata, syphilids, verruca, sebaceous cysts, nevus, furuncles, acne necrotica.

**Tongue.**—Leucoplakia carcinoma, tran it ry benign plaques, burning tongue lingual tonsillitis, syphilids.

**Trunk.**—Dermat tis enenata, infectious eczematoid dermatitis, purpura, seborrheic dermatiti pityriasi rosea, urticaria, herpes zoster syphilis, psoriasis, seborrheic keratosis, scabies, pediculos s exa themata.

## TREATMENT

Treatment to be successful must accomplish aims which themselves depend on a rational plan and the plan depends on correct interpretation of the abnormality to be dealt with. Empirical dermatologic therapy is obsolescent. Only the minority of patients nowadays receive treatment which has been prescribed solely because such treatment has helped other patients with similar troubles.

The cleverest plan of treatment is a failure if the patient is not adequately instructed in carrying it out, or if the patient cannot be so controlled by his physician that he does what he is asked to do. In possibly half the cases the dermatologist sees, cure requires keeping something off the patient rather than putting something onto him or into him. In ordering medication one should not omit the stop order for persistent, unnecessary use of medicines is objectionable and often harmful.

A patient is likely to cooperate if he is told why he is asked to do or take something in a certain way. Intelligence in the patient may be hoped for but cannot be expected. While this fact adds to the physician's difficulties, it adds also to his responsibilities. There is no doubt that rapport, confidence, and encouragement play an important part in delivering that for which the physician's services are engaged. Perhaps much of this discussion could be classified under psychotherapy.

Great trust may be placed in the fact that the living organism tends to heal itself if given an opportunity to do so. Treatment is usually directed at enabling this to happen. In generalities, if the skin is injured by physical agents, treatment comprises prevention of further trauma, prevention of infection, and relief of suffering while the patient heals. If the skin is injured by chemical agents, externally applied or internally absorbed, through direct intoxication or through the effects of sensitization, treatment comprises prevention of further injury by removal or neutralization of the noxa or desensitization to it if possible, prevention of infection, and relief of suffering while the patient heals. If the skin is infected, treatment comprises getting rid of parasites by mechanical, chemical or biologic means, changing the host parasite equilibrium by altering environment or soil to the aid of the one and the detriment of the other, prevention of secondary infection, and relief of suffering while the patient heals. If the skin is disturbed by nutritional defect or metabolic imbalance, treatment may be directed more or less specifically at correction. If the skin is damaged through the mediation of the psyche, much can be done in some cases at least, to alleviate the patient's problem if it is recognized. If the skin is malformed, one selects the most suitable restitution or substitution, or teaches the patient how to live with his deficiency as well as he can. If the skin contains neoplasm, treatment endeavors to destroy all tumor tissue by surgical or radiologic means while respecting the patient's capacity, necessity, appearance and comfort. In diseases of unknown cause, such as psoriasis, lichen planus, pityriasis rosea, lupus erythematosus, and dermatitis herpetiformis, empirical remedies of decided value and some reliability have evolved from the records of trials and

errors which have been accumulated through experience When multiple etiologic factors work simultaneously they must be unraveled and appropriately dealt with

In all therapeutic effort one must remain aware that people with dermatitis are as a class more susceptible than others to intolerance of medication Agents should be chosen for their ability to accomplish good without doing harm Prescriptions should embody the fewest and safest ingredients. One only asks for trouble when one compounds a medley containing the pharmacopoeia and perhaps some nonstandard items and smears it on See Underwood and Gaul (J 138 570 1948)

## INTERNAL TREATMENT

**Antihistamine Agents.**—Benadryl, Pyribenzamine histadyl, and others have been introduced in the past few years and are notably effective in palliating urticaria, asthma and hay fever See Council Report (J 132: 702, 1946); Epstein (WisMJ 45: 489 1946); O Leary and Farber (J 134: 1010 1947) Osborne et al. (ADS 53: 309 194 ); Lee et al. (JPhE pT 90: 83 1947) histadyl. Acute urticaria is particularly well relieved, and most cases of chronic urticaria are helped. Physical allergy of urticarial manifestations is relieved. Other itchy dermatoses contact dermatitis dermatitis herpetiformis, lichen planus and the like are sometimes palliated. The dose approximates 50 mg each 8 hours, but may be diminished or increased according to the patient s response Intolerance phenomena occur see Dermatitis medicamentosa.

Benadryl, β dimethylaminoethyl benzhydryl ether hydrochloride is a white crystalline water soluble synthetic antispasmodic of some use in palliation of urticaria (Shaffer et al. ADS 5 43, 1943) Pyribenzamine may be more effective

**Antimony** has proved efficient in the treatment of granuloma inguinale and leishmaniasis Fuadin is a valuable preparation of trivalent antimony

**Arsenic**, when prescribed in the form of liquor potassii arsenitis, sodium cacodylate or arsenious acid, is largely excreted by exfoliation, for it becomes attached to epithelial tissue When given over long period of time even in small doses, arsenic may cause pigmentation and arsenical keratoses.

SODIUM CACODYLATE (sodium dimethylarsenate) is worthless as a spirocheticide but is useful in dermatitis herpetiformis.

ARSENICALS.—Many possess specific treponemicidal properties. Chief among these are arsphenamine neoarsphenamine sulfarsphenamine Bismarsen, acetarsone, and Mapharsen. The object in compounding the agent is to secure a preparation of maximum injurious effect on the invading organism and minimum evil effect on the host These are tonic in many disorders as well as efficient in the treatment of syphilis (pp. 761 ff) Toxicology is discussed on p. 101

**Autogenous Serum and Foreign Proteins.**—For autohemotherapy, some 10 c.c. of blood from the cubital vein is reinjected at once intramuscularly Or serum after centrifugation may be used in place of the whole blood. From 3 to 10 injections are given at intervals of from 3 to 5 days Various dermatoses may be treated in this way though the value of the method is doubtful

Foreign protein in the form of typhoid or other vaccines and various other substances sometimes yield benefit in a manner ill understood in psoriasis, urticaria, pruritus, and dermatitis of unknown cause Foreign protein therapy is dangerous and often harmful in lupus erythematosus and pemphigus. (Cecil and Hektoen J 103 1 03 1846 1933.)

**Aureomycin.**—See lymphopathia venereum and Dryer et al. (J 139: 117 1949)

**Bacteriophage** may have some value (Combes NYSJM 4 1143, 194 )

**BAL, British Anti-Lewisite**, 2,3-dimercaptopropanol, is a dithiol which reactivates an arsenic inhibited pyruvate oxidase system and so detoxifies trivalent arsenical poisoning as well as poisonings with other heavy metals. Its administration is followed by marked increase of arsenic excretion in the urine The 10 per cent oil solution is injected intramuscularly each 4 hours for 4 doses of 0.5 cc /30 pound body weight. Toxic reactions may occur but are preferable to arsenical encephalitis or dermatitis, which BAL may cure See Peters (Nature Nov 25 1943) Waters and Stock (Sc 102: 601, 1945) WDTBM 101 104 (Oct., 1944) Sulzberger and Baer (J 133 293 1947)

**Bismuth** causes the rapid disappearance of the spirochete from primary and secondary syphilitic lesions. It is generally superior in its therapeutic properties to mercury It cannot be relied on as the sole antisyphilitic drug (Walsh and Becker: *J 116*

434, 1941.) Bismuth is also used in the treatment of lichen planus, lupus erythematosus and warts (q.v.). While the subsalicylate in oil suspension is the usual preparation, Thiobismol and Bismarsen (Beerman et al.: J 120: 333 194..) are also popular.

Bismuth compounds which differ in solubility differ in rapidity of absorption and excretion and in duration of action. If continued action is desirable too rapid absorption would necessitate frequent injections, and slow absorption might delay the effect and tend to produce cumulative toxicity. Oil-suspended bismuth subsalicylate shows slow but continued absorption. Most of the clinical toxic symptoms, including stomatitis, dermatoses, and nephrosis occurred with this preparation (Cole et al.: AmJS 23: 143, 1939).

The usefulness of a bismuth preparation involves the concentration of active bismuth in the tissues, and the height, course, rise duration, and decline of this concentration. The more prompt absorption of the watery solution tends to remove them from the site of injection and to empty the absorption depots, so that the concentration of bismuth is not maintained with weekly administration. Oily solutions are essentially similar to watery solutions in their absorption, but they differ in practice because they are injected in higher doses, so that weekly injections suffice to produce high and lasting absorption. It is therefore not necessary to inject them more often than weekly. Additionally advantageous is the fact that they usually produce less local irritation than watery solution. For its use in syphilis, see p. 763.

Toxicity and tolerance depend on the content of elemental bismuth and its rate of reaching the blood, so that intravenous administration is dangerous (Clausen: JPhExpT 76: 338, 1942).

Sobisminol mass and Bistrimate for oral administration are absorbed in therapeutically active concentration. Lacking the dangers of injections, they have great utility (Kay and Fri ker: CalWM 50: 348, 1939. Howles: BMJ 41: 1033, 1948).

**Calcium.**—Coagulability of the blood is perhaps diminished in a number of cutaneous disorders, particularly urticaria, pernio, and purpura. Calcium salts may be given to overcome this deficiency. Seldom indeed have we seen benefit resulting from their use either by mouth or intravenously.

**Cathartics and Diuretics.**—Saline laxatives are usually to be preferred. Magnesium sulfat (ʒi) is less palatable than magnesium citrate. Milk of magnesia (ʒi ii) is effective. Aromatic fluidextract cascara sagrada practically never causes a rash. Mineral oil and the more elegant proprietaries are useful. Calomel (gr i ii) is drastic but effective. Bad bowel habits, fatigue and hypothyroidism are among the common causes of constipation. Many patients may advantageously increase the ratio of fruits and vegetables in their diets. We often give the advice to go to bed earlier, get up earlier and allow a quarter hour of leisure in the morning for evolution of an urge to stool; also we advise missing a day is rarely fatal.

**Chloromycetin.**—See Streptomycin, p. 156; Edit (J 138: 432, 1948).

**Ephedrine** has pharmacologic properties similar to epinephrine but the duration of its effect is relatively prolonged, and it is active when given by mouth.

**Epinephrine**, potent vasoconstrictor, is of value in urticaria.

**Gold** preparations, especially gold sodium thiosulfate have been found useful in dermatology. Lupus erythematosus and certain tuberculids may respond favorably.

**Histaminase**, available as Torantil is an enzyme which destroys histamine, the toxic substance thought responsible for anaphylactic responses. Perhaps it has value in serum sickness and hives. (Laymon and Cumming: JIn D 3: 301, 1939.)

**Iodine and the Iodides** internally are used in syphilis, sporotrichosis, blastomycosis, and actinomycosis. Iodides are not spirochetecidal. The potassium salt is given by mouth, the sodium salt intravenously. Externally tincture of iodine which may be diluted 1:5 with alcohol, is a valuable antiseptic.

**Iron** is of dermatologic value mainly for sore tongue due to secondary anemia. Large doses must be given.

**Lipocaic**, Dragstedt pancreatic extract which diminishes cholesteremia and aids fat metabolism, has been alleged to help psoriasis, but seems to us dermatologically valueless. (Rowlett and De Kay: RMtMJ 37: 347, 1940. Walsh: *JIn D 4: 59, 1941.*)

**Liver extracts** have their place in treatment of dermal manifestations of certain anemias and avitaminoses. Their preparation was clarified by Teeter (J 127: 973, 1945). They are used in hepatic deficiencies and some intoxication such as arsenical dermatitis.

**Mercurials** are valuable in the treatment of syphilis (p. 761) and lichen planus. The protiodide by mouth the salicylate in oil intramuscularly and the ointment by inunction are the common preparations.

**Parathyroid Extract** is sometimes useful in calcinosis, prurigo, and papular urticaria. (Albright: J 117: 5 7 1911)

**Penicillin**, discovery of which is credited to Fleming (BJExpP 10: 226 1929) and early tried in human disease by Abraham et al. (Lancet : 177 1941) has changed the practice of dermatology The penicillins all have the empiric formula $C_9H_{11}O_4SN_2R$, R being variable (Sc 102 627 1945) All are strong monobasic acids, readily deteriorated by heat acid and oxidation. Parenteral administration results in 60 per cent urinary excretion, oral only 14 per cent so that 3 to 5 times as much must be given by mouth as by injection to accomplish the aim (Frei et al.: Sc 10? 606, 1945) Serum concentration can be increased significantly by restriction of water intake and the administration of 2.5 gm. benzoic acid and 0.5 gm. sodium chloride each 4 hours while penicillin is being given (Bronfenbrenner and Favour: Sc 101: 673, 1945) and in other ways such as by using caronamide in a dose of ? to 3 gm. each 4 hours (Crosson et al. J 134: 1528 1947; Sweet et al.: BMJ 41: 326, 1948)

Pure preparations are now available in quantity Penicillin G was synthesized by du Vigneaud et al. (Sc 101 431 1946) Applications of gauze sopped in culture fluid f P notatum are obsolete though interesting as well as curative in their time (Robinson and Wallace Sc 98: 329 1943) Urticaria, commonly provoked by oral administration and less commonly by parenteral, is less frequent nowadays (see dermatitis medicam ntosa p. 107) No sequential intoxication has been reported only rarely even from huge doses. Penicillin is relatively safe, while sulfonamides are not. There is little the latter can do that the former cannot do as well or better except to penetrate i to the cerebrospinal fluid.

Penicillin is effective syphilis yaws, pinta, gonorrhea meningitis (where sulfonamides are preferable) almost all treptococcic infection most staphylococcic infections, anthrax diphtheria, Vincent s disease infective exfoliative dermatitis, and some cases of sycosis and etmoth coris. Topically its effect is superficial. While a thimbleful of ointment containing 200 units per gram ften suffices to cure impetigo, infectious eczematoid dermat tis requ res parenteral and often high dosage

Penicillin is not effectual in pemphigus psoriasis, erythema multiforme lichen planus, lupu erythematosus, tuberculosis, blastomycosis, tinea, acne scabies, urticaria, contact dermatiti (unless secondarily infected which is frequently the case) and a multitude of other illnesses. When focal infection causes persistent dermatitis, usually acral the effect of penicillin is of temporary benefit only

It is scientifically desirable to test the sensitivity of organisms cultured from a patient to penicillin in vitro but clinical results do not invariably parallel the findings. The practit oner is likely to cure a patient before the laboratory renders its report Because of speedy excretion, it is desirable to give penicillin by injection each 3 hours. Practitioners know that many a patient has gotten well when supplied with a vial of solution, a syringe and needles, and instructions to stick it into himself in a dosage of ?0,000 to 50,000 units 3 to 5 times in 24 hours. The oil emulsion of 300,000 unit given daily is a practical and advantageous procedure. Preparations effective fo more than ?4 hours are being developed (Sullivan et al. Sc 107 169 1948) An injection of procaine penicillin G with aluminum monostearate per cent may yield effective blood levels fo 96 hours.

Oral administration in effective dosage is expensive and at present impracticable in general, except in infants, to whose formula penicillin may be added in adequate and harmless dosage Topically the lozenges may help a stomat tis.

For local use proprietary ointments containing 250 to 1 000 units per gram are readily available. An excellent prescription which retains its potency satisfactorily is:

℞

| | |
|---|---|
| Penicillin | 100,000 units |
| Water | 20.0 c.c. |
| Lanolin | sufficient to mix |
| Petrolatum | to make 250.0 gm. |

The physician may stock this in his refrigerator and dispense half an ounce or so at a time economically Half an ounce is what is usually needed to manage a case of impetigo. The strength is adequate; too strong a concentration will cause primary irritation within a few days. See Waisman and Gots (ADS 53 234 1946) Cormia and Alsever (Ib. 54: 136, 1946)

Intolerance of penicillin is commonplace (see dermatitis medicamentosa), and the chemical should be reserved for use when it is indicated and necessary. Saline solution of crystallin penicillin G seems less often provocative of rashes than the oil emulsion. We look at patients' feet before we start the chemical and try to avoid its use if tinea is present. See Morginson (J 132: 915, 1946)

Sulfonamide and penicillin may be given simultaneously to advantage, for the former acts by bacteriostasis and the latter is bactericidal especially at the time of cell division (Hobby and Dawson. JBact 51: 447, 1946)


Cohen, T. M., and Pfaff, R. O. ADS 51: 172, 1945 (miscellaneous skin cases)
Davies, J. W. T. et al. QJM 14: 183, 1945 (aqueous spray 1,000 U./c.c.)
Franks, A. G. et al. ADS 52: 14, 1945 (topical and intramuscular)
Garber, L. H. et al. J 130: 761, 1946 (booster doses to reach foci)
Goldberg, L. C. ADS 53: 184, 1946 (topical, 500 U./gm.)
*György, P. et al. PaMJ 49: 403, 1946 (oral)*
Hellier, F. F., and Hodgson, G. A.: Lancet 2: 402, 1945 (spray, 250-500 U./gm.)
Morginson, W. J. BMJ 2: 320, 1945 (miscellaneous skin infections. Vincent's)
Richards, A. N. J 122: 235, 1943 (valuable review)
Romansky, M. J., et al. J 128: 404, 1945 (Seitz filtered, autoclaved peanut oil 96.0 per cent by volume; gauze filtered, autoclaved beeswax 4.0 per cent; calcium penicillin 100,000 U./c.c. of vehicle blended mechanically. One dose 300,000 units per 24 hours, prolonged absorption; no local sequels.)
Roxburgh, I. A., et al. BMJ 1: 524, 1944 (miscellaneous)
Taylor, P. H., and Hughes, K. E. A. BMJ 1: 699, 1944 (spray 1,000 U./c.c.)
Templeton, H. J. et al. ADS 51: 305, 1945 (local use valuable only in superficial disease)
Syphilis, Penicillin in: J 130: 677, 682, 688, 694, 698, 1946 (action on *T. pallidum*; pregnancy; congenital; early; cerebrospinal)


Pituitary derivatives have been used to encourage the growth of hair. Pituitrin may relieve the pain of herpes zoster.

**Salicylates.**—Aspirin is a valuable sedative and analgesic.

**Sedatives.**—Opium is as a rule of little value in diseases of the skin. It frequently increases pruritus. Bromides are not satisfactory being prone to intoxicate. Barbiturates depress the emotions and promote a desire to sleep but in the itching patient, this is not the aim, for the patient would sleep if he were relieved of his itching. Aspirin (gr. v-x each 3 hours) may be taken freely to secure rest; rarely it causes urticaria or asthma. Aminopyrine (gr. v-xv) is useful. Pruritus is best controlled by local applications. The avoidance of caffeine (coffee, tea, and some carbonated beverages) is often sufficient in itself. Benadryl has a useful sedative effect.

**Sex hormones,** including male, female, and gonadotropic, have utility in some conditions. They are potent substances, as pointed out by Kepler and Randall (MCNAm 24: 941, 1940) and can cause trouble. Estrogenic substances in correct dosage may help rosacea and some cases of acne. They are necessary in keratoderma climactericum.

**Splenic Extract,** often given for nonspecific desensitization, seems to us to be worthless.

**Sodium Thiosulfate,** commercially photographer's hypo, has been used widely and with good effect in metal intoxications, especially arsenic. It is alleged to help contact dermatitis and to be a general detoxifier which we do not believe. Externally the salt has utility in prophylaxis of tinea, and in treatment of iodine burns.

**Streptomycin,** an antibiotic from *Actinomyces griseus,* inhibits *E. coli* and many other gram-negative bacteria, as well as some gram-positive ones and various fungi (Waksman, quoted J 126: 103, 1944; 129: 1096, 1945). Parenteral injection is effective, and excretion is largely urinary. A unit is about 0.06 time as effective as a unit of penicillin. Zintel did not have alarming or late toxic results from large doses in man (AmJMSc 210: 42, 1945). Its value in dermatology is great in the treatment of tuberculosis, tularemia, and chancroid. See Marshall (*MTimes 74: 337, 1946*). It may damage the eighth nerve and cause rashes.

**Sulfonamides.**—Sulfanilamide, p-amino-benzene sulfonamide, is a derivative of red dye. Erysipelas, scarlet fever, chancroid, chronic acrodermatitis, lymphogranuloma venereum, gonococcal infections, and other bacterial dermatoses are often astonishingly responsive to sulfanilamide therapy (Strickler and Stone: ADS 40: 244, 1939). Sulfanilamide is usually tolerated in doses of one to three 0.5 gm. tablets t.i.d., or in even larger quantities (see dermatitis medicamentosa, p. 109). Sulfapyridine, (p-amino-benzene sulfonamide) pyridine, is remarkably effective against the same infections as sulfanilamide, but causes nausea in small dosage. Sulfathiazole, anti-streptococcic and to some extent antistaphylococcic, is another valuable sulfonamide medicine. Sulfadiazine is probably the safest. The utility of these, welcome as they were a few years ago, has largely been superseded by penicillin because of the dangers entailed by sulfonamides (see dermatitis medicamentosa). Most dermatologists disapprove the topical application of sulfonamides in any condition.

**Thyroid Extract** is specific in hypothyroid states, and proves beneficial in acne sometimes in xanthoma psoriasis, and dry scaling dermatitides. Its administration diminishes lipemia.

**Toxoid Therapy**—Staphylococcus toxoid is the formol-treated filtrate from bouillon cultures of staphylococci. It increases the antitoxin titer of the blood, yet produces no serious untoward symptoms (Anderson and Stokes: ADS 40 582, 1939. See also J 101: 582, 1933.)

**Tyrothricin**, an antibiotic from a soil bacillus contains gramicidin and tyrocidine. It is soluble in alcohol but not in water is valueless orally and poisonous by injection. Active against gram-positive organisms, the 0.3 per cent emulsion topically seemed responsible for cure of 5 of 6 leg ulcers reported by Rankin (AmJS 65: 391 1944). An interface active vehicle was recommended by MacKee et al. (JInvD 7: 173, 1946). We consider this antibiotic quite disappointing in dermatologic practice.

**Vaccine Therapy** is often used in furunculosis carbunculosis, infectious eczematoid dermatitis, and dermatitis repens. In acne and sycosis, results are dubious. Typhoid vaccine is useful as a means of provoking fever artificially. Frei antigen is important in the therapy of lymphogranuloma inguinale.

**Vitamin** concentrates have proved their efficacy in the relief of conditions due to their inadequate supply or utilization (See p. 431.)

## EXTERNAL TREATMENT

**Prescriptions** are listed in the index.

**Local Applications** employed in dermatology can be classed as to form of application and pharmacologic purpose. Remedial agents may be prescribed in the form of baths, compresses, dressings, lotions, ointments, pastes, powders, or plasters. Their purposes are cleansing, soothing, protective, astringent, antipruritic, antiseptic, keratolytic, reducing, stimulating or escharotic. *Physical agents as well as medicaments are used.*

**Cleansing**.—*The soft water bath with a reliable nonirritating soap is* excellent. Soap baths accomplish débridement and in dermatology are prescribed with detailed instruction as other medicines are. They are necessary in scabies to enable parasiticidal agents to get at the mites, and the average case of tinea of the feet can be cured by elevation, aeration and the proper use of soap for the removal of excess corneum. Soap must be rinsed off thoroughly. The typical hospital bath inflicted upon bed patients with washrag and a small basin of water causes much irritation.

Saturated fatty acids of low molecular weight more often give positive patch tests than those of higher molecular weight. Reaction to castor oil is rare. Irritation by soaps is not directly related either to the alkali or the fatty acid component alone. Some fatty acids at pH are more irritant than others at pH 5. A detergent composed of 25 per cent sulfonated oil, 25 per cent liquid petrolatum, and 50 per cent water at pH 6.5 proved excellent in replacing soap, but relapse of dermatitis occurred when the use of soap was resumed, as reported by Blank (ADS 39 811 1939); see also *Lane and Blank* (*J 118 804 194* )

Cationic soaps is the term applied to germicidal and cleansing detergents in about 1 per cent aqueous concentration (J 1 4 700 1944). They leave an imperceptible yet strongly germicidal film on the skin and may be of some use (Miller et al.: PSE pB 31 1 4 1943)

**Soothing, Protective and Antipruritic Applications**.—Relief of irritability is often accomplished by dressings to exclude air, mild astringents, or the use of lotions. In most oozing itching dermatoses, wet dressings of aluminum acetate (1 gm. per 1 000 c.c. of water) or potassium permanganate (1 5 000) offer considerable immediate relief.

Burow's solution has long been a popular astringent lotion in the treatment of burns and oozing dermatoses.

| | | |
|---|---|---|
| ℞ | Aluminum sulfate | 5.0 |
| | Lead acetate | 25.0 |
| | Water | 500.0 |

Sig.: Astringent lotion; dilute as required to avoid irritant effect.

Goulard's extract (20 per cent lead acetate in water) when diluted 1:50 is good in moist compresses.

Dalibour water is another astringent similarly used (see Anderson (SouthwestM 23 336 1939) and Sézary (YBD 1939 p 463)

| | | |
|---|---|---|
| ℞ | Copper sulfate | 1.6 |
| | Zinc sulfate | 5.6 |
| | Camphor water | to 240.0 |

Sig: Teaspoonful to half pint of water for moist dressings.

Pick's liniment forms a translucent jelly which dries as a film

| | | |
|---|---|---|
| ℞ | Tragacanth | 5.0 |
| | Glycerol | 5.0 |
| | Water | 100.0 |

Mix with grinding. Label Pick's liniment.

In contact dermatitis, one hesitates to apply any chemical when it is not known whether the patient is susceptible to irritation by it. We find useful a procedure of applying plain white petroleum jelly and over that clean soft towels moistened with cool water plain or isotonic with table salt in it, a dram to the quart. An irritated skin will in a few hours or days return to normal, if further irritant contact has been prevented.

Calamine lotion has a drying effect

| | | |
|---|---|---|
| ℞ | Phenol | 1.0 |
| | Starch | |
| | Zinc, oxide, | |
| | Prepared calamine of each | 20.0 |
| | Glycerin | 10.0 |
| | Water | to 200.0 |

Sig. Carbolized calamine lotion. Shake and apply t allay itching.

Calamine lotion may be modified by the incorporation of various substances such as alcoholic solution of coal tar or 0 05 per cent bichloride of mercury Bentonite, a clay may be put in the vehicle, though tragacanth is as good. It is common knowledge that calamine is zinc oxide contaminated with iron oxide, which is harmless. Experimentation with red, brown and black iron oxides will enable one to match his lotion to the complexion on which it is to be applied.

All soaps are alkaline. Since alkali tends to cause dissolution of epidermal cells, soaps are contraindicated in acute dermatitis, especially eczematous (Parkhurst ADS 43 298 1941)

Soda baths and tar baths are sometimes employed in the treatment of psoriasis and chronic dermatitis. The continuous bath is advisable in some cases of pemphigus and extensive burns. The permanganate bath is valuable. Proportionately smaller quantities may be made up for soaking an arm or leg the hands or feet or as a douche in the treatment of mycotic vaginitis with pruritus vulvae

| | | |
|---|---|---|
| ℞ | Potassium permanganate | 6.0 |
| | Water | 100.0 |

Sig Six per cent $KMnO_4$ solution. Two ounces to 10 gallons of tepid water for baths. One (or two) teaspoonfuls to a quart of tepid water to soak hands or feet 15 minutes b.i.d. (or for daily douche)

The oatmeal bath is often soothing and comforting in widespread dermatitis or urticaria. A cup of oatmeal boiled to a jelly is poured into a cloth sack over the drawn tub of water at 100 F The sack is tied tightly and squeezed about in the water it prevents the oatmeal from stopping the plumbing

Starch baths are made by cooking 2 cupfuls of cornstarch (laundry starch contains borax and often irritates) until it is soft This is added to a tub of cool water along with Sweitzer recommends, a cupful of baking soda.

Aluminum acetate powder a dessertspoonful to 15 gallons of tepid water *followed by dusting with cornstarch, is soothing and antipruritic.*

Bichloride of mercury 1 12,000 (5 gm. or ten 7½ grain tablets in 15 measured gallons of water) provides a valuable though somewhat hazardous antiseptic and astringent bath useful in widespread infectious dermatitis. One must learn how to use and when to stop such baths. Absorption when the epidermis is much eroded results in mercurialism with diarrhea or worse, and many a skin does not tolerate mercury at all

Highly alkaline soap such as sapo viridis, may be desired for its keratolytic effect in psoriasis, seborrheic dermatitis, or acne Medicated soaps possess little added germicidal value and are frequently irritating (J 124 1195 1944)

*Scales and crusts may be removed by means of petroleum jelly olive* oil or starch poultices Benzine is effective for cleansing oily greasy surfaces and removing adhesive plaster A good cleansing antipruritic lotion is Pusey s liniment

| | | |
|---|---|---|
| ℞ | Phenol | 1.3 |
| | Powdered tragacanth | 4.0 |
| | Sodium benzoate (a preservative) | 0.5 |
| | Olive oil | 150.0 |
| | Water | t 480.0 |

Sig Soothing lotion. Apply freely to allay itching

A principle often overlooked is that it is as necessary to stop a medicament *as to start it A healed skin is a normal one, which requires on it* nothing at all

**Dusting Powders** generally consist in the main of cornstarch, zinc oxide zinc stearate, calamine, and boric acid

| | | |
|---|---|---|
| ℞ | Zinc oxide | |
| | Zinc stearate | |
| | Talc | each t 60.0 |

Sig. Bland dusting powder

One may add antipruritic or antiseptic chemicals to this, such as camphor 2.0 gm.

*Ointments have a wide sphere of usefulness. They consist of lipids* of various kinds, perhaps emulsified in which divers medicaments are suspended or dissolved White petroleum jelly is the common vehicle but is not penetrant. Cholesterinized bases are more penetrating Lanolin (wool fat) takes up watery solutions and is on that account a useful vehicle. Vanishing creams are watery emulsions composed mainly of higher fatty acids.

Ointments are generally not used if weeping exists. The addition of starch thickens an ointment into a paste and enhances its power to

take up secretions. Ointments smeared over staphylococcic dermatoses succeed only in spreading the disease.

Rose water ointment is the U.S.P. cold cream.

Many ointment bases are available, some proprietaries possessing some elegance. We think no great advantage accrues from their use except the recognized virtues of a polyethylene glycol, Carbowax, which is water soluble and especially welcome in applying medication to the scalp from which it is easily washed out (Maynard: JInvD 8: 223, 1947; Hopkins: ib 7: 171, 1946). Vehicles, their physical, chemical and functional characteristics, were fully discussed by Lane and Blank (ADS 54: 497, 650, 1946). We never prescribe complicated vehicles; we judge them overrated.

**Surface Active Agents** for wetting, penetrating, emulsifying, dispersing, solubilizing, foaming, and washing have occasioned much dermatologic interest (Specl: JInvD 6: 223, 1945; Dunneling: ADS 43: 264, 1941). The molecule of the wetting agent generally contains water-soluble (hydrophilic) and also lipid soluble (hydrophobic) groups, because of which it becomes oriented at an interface and lowers surface tension. Methods of cleansing and protective applications and formulas utilizing some of these were discussed by Klauder et al. (ADS 41: 331, 1940). Much industrial dermatitis is caused by cleansing agents. Schwartz (PHRpts 56: 1788, 1941) commended sulfonated castor oil 50, vegetable oil 48, and a wetting agent such as Duponol 2, as a soapless cleanser for industrial use. Accepting the utility of cleansers dependent on these for their effectiveness as substitutes for, and often improvements upon, soaps, which are common causes of dermatitis, we are nevertheless hesitant to recommend them highly as adjuvants of theory. We are perhaps naively pleased with the results of treatment in which few bases are prescribed other than petrolatum and lanolin. It is true that penetration can be enhanced by the choice of vehicle (MacKee et al.: JInvD 6: 200, 1945; 7: 43, 1946) and occasionally this is necessary. A typical nongreasy ointment base (Downing et al.: ADS 50: 8, 1944) of cosmetic elegance capable of being washed off easily is:

| | | |
|---|---|---|
| R | Sodium lauryl sulfate | 0.8 |
| | Cetyl alcohol | 15.0 |
| | Glycerol | 5.0 |
| | White petrolatum | 14.0 |
| | Water | 25.0 |

**Protective Ointments**, while low on the list of preventive measures, are often the only available means of protection. In other instances they protect the skin from irritants which may escape into the air in spite of other preventive measures. The face cannot be covered by protective clothing and often the work must be carried on with bare hands. When a protective ointment is used, the worker removes it with soap and water after work and so removes at the same time whatever irritants are on the skin. This adds considerably to the protection supposedly given by the ointment. (Schwartz: MCNAm 26: 1195, 1942, giving type formulas and composition of industrial protective creams and cleansers.) Varieties include vanishing cream facilitating removal of soil when washing, invisible glove films which may be water-soluble or water insoluble, fatty water repellent ointments, ointments containing nonirritant chemicals detoxifying specific irritants, ointments serving as vehicles for inert powders which form protective covering, and agents protective against photosensitization. Lanolin and petrolatum afford more secure protective films than other substances do and addition of powders to them diminish their protective efficiency (Mason and Schwartz, 1946).

Ointment prescription and effect and the influence of pH were discussed by Henry (BJD 34: 1, 194 ).

**Zinc Oxide Ointment** (zinc paste) does not absorb water but possesses some antiseptic power (Strakosch: ADS 49: 8 1944). An emulsion base may be prescribed, however.

**Lassar's Paste** contains zinc oxide 25, cornstarch 25, petrolatum 50. To it 1 to [illegible] per cent salicylic acid [illegible] may be added, as well as 0.5 to 1 per cent phenol. It is a thick protective antipruritic substance of considerable utility.

**Peloids** (muds, [illegible]) have physical effects of some interest (Singer: J [illegible] 431 1944). Bentonite, a hydrated aluminum silicate, [illegible] is a detergent and dispersion agent incompatible with acids and inorganic acid salts. It is prescribed by some dermatologists (Goodman: ADS 49 [illegible] 1944).

**Boric Acid Ointment** is losing popularity because of its possible toxicity (Pfeiffer et al.: J 1[illegible]: [illegible] 1943). We consider cod liver oil ointment to possess a remarkable virtue (see J 1[illegible]: 750 1942).

**Ichthyol** is a bland and soothing sulfonated bitumen of complex chemistry, a tarlike substance of considerable popularity (Stewart et al.: ADS 45: 933 1942). **Naftalan** is somewhat similar in appearance and use. These are prescribed in an ointment base in a concentration of 10 to 20 per cent for various manifestations of dermatitis.

**Phenol** is the most reliable antipruritic in a strength of from 0.5 to 2 per cent. Menthol evokes a sensation of coldness. Some synthetic topical anesthetics, such as orthoform and cycloform, prove serviceable at times. Ethyl aminobenzoate (anesthesin) in 2 to 3 per cent strength is helpful in combating intolerable itching.

**Coal Tar**, crude or in the alcoholic solution, is a valuable antipruritic. Crude coal tar is extremely valuable in the treatment of infantile dermatitis, lichen chronicus simplex and other pruritic disorders. A good prescription is White's:

| | | |
|---|---|---|
| R | Crude coal tar | 3.0 |
| | Lanol | sufficient to mix |
| | Zinc oxide | 6.0 |
| | Petrolatum | to 100.0 |

Sig.: 3 per cent coal tar ointment

**Zetar*** is miscible in water and effective therapeutically (Combes: ADS 56: 583 1947).

**Keratolytics** are agents for dissolving the corneum. Salicylic acid, resorcinol and alkalies are of this class. The keratolytic action of soaps is due to alkali. These find their usefulness in hyperkeratotic conditions such as ichthyosis and scaly tinea.

**Reducing Substances** hasten keratinization and influence favorably such diseases as psoriasis and seborrheic dermatitis. Cornbleet (ADS 33: 625, 1936) found the ability to reduce methylene blue greatest in dihydroxyanthranol (Anthralin or Cignolin, see J 124: 647 1944) while in order of diminishing potency were chrysarobin, pyrogallol, juniper tar, crude coal tar, precipitated sulfur, coal tar solution and ammoniated mercury.

Chrysarobin is a medicine the dermatologic aspirant must learn to use skilfully. On the skin it is oxidized to oxychrysarobin, chrysotoxin, and chrysophanic acid, the first being therapeutically active and the last not. Petrolatum is the best base although chloroform is also a vehicle suited to certain purposes. Its application induces erythema followed by peeling and it is a classic agent in the treatment of psoriasis and dermatomycoses. In the eye, which it may reach through misadventure, it provokes violent

* Dermik Pharmacal Co.

and hazardous conjunctivitis and keratitis. Hence it is rarely put on the scalp and is prescribed invariably with the warning to keep it from the face. A potent reducing agent, its action is neutralized promptly by potassium permanganate. Chrysarobin conjunctivitis treated with frequently repeated washes of the antidotal 1:5 000 $KMnO_4$ is not the fearsome complication it has been thought to be (Strakosch ADS 49: 1 1944) A sophisticated patient can use it on the scalp safely

Sulfur probably exerts little influence except upon the odor of the stools when taken internally It has been given in nail dystrophies. Externally it is a valuable antiparasitic Its effect on the skin seems to be due to the formation of persulfides in the presence of the sulfhydryl radical present in cysteine and glutathione in the corneum. Petrolatum is better than an emulsion base in promoting the keratoplastic action of sulfur The keratolytic effect of salicylic acid with sulfur is better than that of either drug alone, the base being not important. (Strakosch ADS 47 216, 1943 48 384 1943) A thick paste composed of 30 to 50 per cent sulfur in petrolatum has antiphlogistic, reducing, antipruritic and parasiticidal influences useful in treating seborrheic dermatitis, pityriasis rosea rosacea, psoriatic erythroderma, and other diseases, according to Abramowitz (ADS 40 823, 1939 NYSJM 43 746 1943) who stated that such concentrations are less irritating than weaker ones and seldom provoke sulfur dermatitis.

**Vioform,** an amorphous powder with the formula 5-chloro-7 iodo-8-hydroxyquinoline long used as a dusting powder in chronic granulating wounds and for trichomonad vaginitis, possesses in 3 per cent concentration in petrolatum great virtue as an antiseptic in eczematized dermatoses such as exudative intertrigo sycosis, and mixed coccic dermatitis (Sulzberger YBD 1946 p 16 Reque Mississippi Doctor Nov 1947) It sometimes irritates (Saunders ADS 54 456 1946) stains things yellow is not tolerated by persons sensitive to iodine and is incompatible with coincidentally applied sulfur or mercurial medication yet it is a significant dermatologic medicament which we prescribe almost daily

**Salicylic Acid,** hydroxybenzoic acid, has the property of separating swelling and macerating keratinized epithelium It is a useful antiparasitic substance. It is antipruritic in from 1 to 2 per cent concentration in an ointment. An alcoholic solution is frequently prescribed in seborrheic dermatitis and tinea. As the active ingredient in Lassar s paste it serves as a nonirritant antipruritic medicament effectual in an assortment of conditions. Salicylic acid reinforces the action of sulfur On corns 40 per cent plasters may be used.

**Resorcinol,** meta-dihydroxybenzene is as useful as salicylic acid and similar in its properties. Its action is keratolytic and irritant (Strakosch ADS 48 393 1943) It stains blond hair reddish. **Euresol,** a proprietary resorcinol monoacetate is often prescribed in a lotion for dandruff

**Gentian Violet,** a pararosaniline dye (pyoktanin blue is an old, proprietary name for this) and the closely related **methyl violet** and **crystal violet,** are deeply staining nonirritant nontoxic substances which evince especial affinity for gram positive parasites Available inexpensively in crystalline form, gentian violet is soluble in water alcohol and chloroform but insoluble in petroleum fractions. It is an excellent parasiticidal local application. (Sutton J 110 1733 1938.) **Acriflavine, brilliant green, carbol fuchsin, and scarlet red** are also valuable antiseptic dyes.

Council Report J 121 26 1943) Ultraviolet treatment has special value in tuberculosis of the skin (q v) and peeling doses cure pityriasis rosea and alleviate acne temporarily Combined with tar ointment, it is a standard treatment of psoriasis (q v) but otherwise its indications in dermatology are few (Cleveland: CanadMAJ 37 558, 1937)

Locally, satisfactory results are obtained from the use of 500 to 1,000 watt incandescent lamps in impetigo contagiosa and similar disorders. The effects are probably due to radiant heat.

**Roentgen Therapy**—X rays produce degenerative changes in all tissues. Their effect is apparently proportional to the mitotic activity of the cellular structures. The epidermis and its glands are first to exhibit appreciable changes. If the dose is pushed beyond a certain point erythema followed by atrophy develops. Untoward results range from this slight manifestation to necrosis of the skin.

DOSAGE.—For the rough estimation of the dosage of unfiltered radiation, Andrews used the formula

$$\frac{\text{current} \times \text{peak voltage squared} \times \text{time}}{\text{distance squared}}$$

and substituting experimentally determined numerical values he stated that, with a particular apparatus, an exposure involving 2 milliamperes, 100 kilovolts (a spark gap between points of about 6 inches) and 3 minutes exposure at a distance of 8 inches produces mild erythema.

Doubling the milliamperage doubles the dose

Doubling the duration of exposure doubles the dose.

Doubling the voltage quadruples the dose

Doubling the distance quarters the dose.

Materials placed between the anode and the recipient skin act as filters, and obstruct the long (soft) rays much more than the penetrant short (hard) rays. Opacity depends on the atomic weight of the material of which the filter is composed. Tissues themselves filter the beam. Since the first millimeter penetrated cuts out a certain percentage of the incident rays of a given wave length, and the next millimeter cuts out the same percentage of the rays that reach it the effect of thickness of filter is to obstruct the energy in the manner of compound interest. Interposition of filters enables a dose to be given which is comparatively uniform in wave length so that only the hardest rays reach the skin, and the beam, being relatively homogeneous is absorbed at a single percentage rate per unit of tissue depth. The *roentgen unit* is that quantity of x radiation which liberates one electrostatic unit of electricity when passing through 1 c.c. of air at standard temperature and pressure. This is the International Standard of x ray dosage and the dose is measured in these units by means of an iontoquantimeter which in simplest terms, is a chamber the contents of which are ionized by the beam of radiation, attached to a charged electroscope the rate of discharge of which by the ionization produced measures the ionization. Variables and complexities entering into the physicist estimation of dosage make the erythema dose (E) a dermatologically practical one Its determination depends on that quantity of irradiation from a particular machine which produces faint but definite redness in a normal skin. The erythema dose at 100 KV peak unfiltered is about 300 (MacKee and Cipollaro ADS 41 1 1940) The E dose increases with increased hardness of the rays, but remains the best standard test of dosage in the opinion of Belisario (ADS 45 611 1942) The half value layer HVL, is that thickness of a filter which obstructs half the energy of the incident beam. HVL increases with increase of hardness About twice the thickness of skin will obstruct the same proportion of radiant energy as a unit thickness of aluminum.

Protection of the operator who should take every precaution to prevent irradiation of himself is described by Taylor (J 116 136, 1941)

The Coolidge tube with tungsten anode and cathode connected to two currents (a low voltage current heats the filament and liberates electrons, and a high potential drives them against the anode) is durable as well as efficient.

DOSAGE COMBINATIONS.—Details of x ray theory and therapeutic technic require more extensive exposition than may be given here MacKee and Cipollaro's *X Rays and Radium in the Treatment of Diseases of the Skin* (Lea & Febiger 1946)

along with the absolute necessity for supervised instruction in the use of roentgenologic machinery combine to render this section inadequate for the practitioner.

Substances, including tissues which are irradiated become themselves a source of secondary irradiation during their irradiation. *Secondary irradiation and back scatter provide a consequential proportion of the dose actually received within the tissues.* On this account the size of the portal through which the rays reach the skin is significant. A larger dose as measured at the skin surface is necessary to deliver an equivalent dose within the *tissues when the portal is smaller*. At 100 KV without filtration added to that which is inherent in the tube the erythema dose variation with the portal area was estimated by Goldberg (ADS 49: 346, 1944) as follows:

| Diameter | F dose | r |
|---|---|---|
| 10 mm. | 1.5 | 310 |
| 8 | 2.3 | 850 |
| 6 | 3.6 | 1200 |
| 4 | 5.0 | 1700 |
| 2 | 8.0 | 2700 |

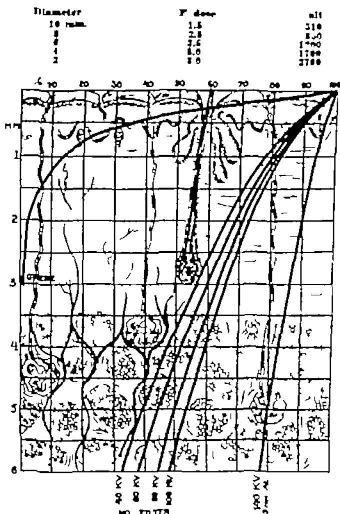


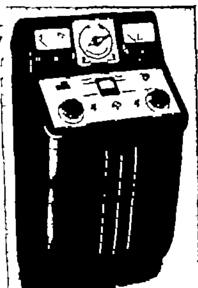

Fig. 47.—Roentgen radiation absorption curves, indicating depth dosage modified by voltage and filtration. (Cipollaro and Mutscheller, ADS 41: 57, 1940.)

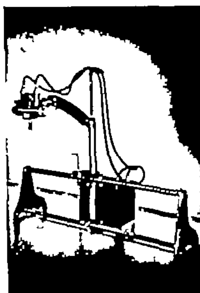
The skin dose received exceeds the air dose measured at the skin surface significantly because of the exit dose which is that part of the incident energy which passes through. The air dose does not adequately express the amount of radiation received by the skin. Applied to the hand, as pointed out by Andrews et al (ADS 50: 333, 1944) at 65 KV skin dose exceeds air dose by 25 per cent, at 100 KV by 45 per cent and at 135 KV with 3 mm Al filtration by 78 per cent.

Other considerations of dosage are elaborated by MacKee et al. (ADS 4 : 490, 657, 1943). A time factor is concerned, for a certain quantity of radiation must be

administered before any cells are destroyed, and cells recover from irradiation so that low intensity of radiation decreases its effectiveness. An area factor is concerned for the erythema is smaller than the mask which determines the portal by about 1.5 mm. for unfiltered radiation and 3.0 mm. for filtered. Therapy apparatus furthermore does not deliver a beam which is uniform in intensity outward from the central ray so that overlapping of fields cannot be done correctly unless the outer rays of the beam as well as the central rays have been calibrated.

Biologic Action of X-rays depends on energy which is absorbed, not on that which passes through. The influence of wave length is negligible. Their effect on tissue is analyzable in terms of effect on cells. The action is necrobiotic, although with small dosage the injury may be subliminal. After a brief latent period shorter with heavy dosage living cells treated with x rays manifest progressive turbidity and granular alteration of the cytoplasm, lose their motility and cease mitotic activity. After a period of inactivity they may resume a normal function, or they may suddenly die; or their granular dissolution may occur promptly if dosage is heavy. Histologically one finds cytolysis, pyknotic degeneration, fragmentation, and vacuolation. Cell types may be listed according to their radiosensitivity in order of greater to less: lymphoid, mucus producing cells of salivary gland and gut, spermatogonia, epithelial, endothelial, young connective tissue, cartilage, muscle, bone, fat, and nerve cells. Bacteria are insensitive and, in general, *doses which would kill parasites would be much more than sufficient to necrotize the tissues of the host.*





Figs. 48 and 49.—An example of modern and excellent x-ray therapy equipment for roentgen treatment of dermatoses. (Courtesy Picker X-ray Corp., New York.)

If one knows how cells react to x rays, and of what kind of cells the skin is constituted, then one can picture the skin with permanent x ray damage: it is a skeleton of acellular fibrotic tissue in which epidermal accessory structures are lacking, capillaries few, fixed tissue cells wanting, and epithelium sickly and thin. See X-ray and Radium Injuries, p. [illegible].

Radiation in Treatment of Dermatoses.—In the following diseases roentgen therapy is especially useful:

Acne
Actinomycosis
Blastomycosis
Bromidrosis
Carcinoma
Favus of scalp
Folliculitis keloidalis
Hemangioma
Hyperhidrosis
Inflammations
Keloid
Lymphoblastomas
Sarcoma
Sycosis
Tinea capitis
Warts

RADIATION IN TREATMENT OF INFLAMMATION.—A furuncle consists of living staphylococci in the central region surrounded by fibrin and by living and dead leucocytes, some of which have engorged some of the cocci. This lesion is set within the dermis, which consists in the main of collagenous and elastic fibers, fibrous cells, blood vessels, and lymph vessels. The damage by bacterial activity is greatest at the center, less peripherally. It suffices to evoke vasodilation (redness) in the outer zone, intracellular swelling and intercellular exudation of proteinous fluid as well as redness in the mid zone, and necrosis at the center. When x rays are applied, the leucocytes dissolve, the capillary endothelium swells, blood flow is obstructed so that redness disappears, the exudate is resorbed, and no one knows what happens to the bacteria. Sometimes the lesion shows exacerbation for a few hours, but the customary clinical effect of roentgen treatment of a furuncle is to cause its prompt disappearance. The effect is similar upon a carbuncle (usually), and is analogous in any other inflammatory disease. Perhaps antitoxic substances are liberated (Hesgard et al.: Radiol. 39: 691, 194.). Cellulitis is favorably influenced (DeHollander: AmJR 45: 531, 1941). See Shaffer (JInvD 3: 159, 1940); Sutherland (AmJMSc 198: 729, 1939); Desjardins (J 116: 225, 1941; Radiol. 38: 774, 194 ). Edit (J 131: 14 4, 1946).

Local sensitivity is abolished temporarily by x rays, seemingly by their effecting the disruption of the cells on which local reactivity depends. The manifestations of contact dermatitis or fungous infection may be made to disappear but respectively the allergen is not removed or the fungus itself remains. When the skin regains its ability to react it does so. The clinical cycle is disease, treatment, cure, recurrence, treatment, cure,—and eventually there results irremediable x ray damage. The same old infection is still superimposed, the more difficult to get rid of, and medicolegal complexities arise.

RADIATION IN TREATMENT OF NEOPLASMS.—There are analogies between the application of radiation and the application of a caustic paste. In either case cure if cure results depends on destruction. In either case one does not know what the exact boundary of the destruction is going to be, and in either case one does not command this boundary but simply intends that it will be sufficient. Excepting in palliation and under uncommon combinations of circumstances we prefer surgical attack if it is feasible, where with a single procedure one takes definitive steps to destroy that tissue which in one's judgment ought to be destroyed, and leaves healthy that which one does not wish damaged. The scar after healing is not an x ray burn.

**Grenz (Infraroentgen) Radiation** designates therapeutic electromagnetic vibrations ranging in the spectrum between the usual roentgen rays and the ultraviolet rays. Wave lengths are used longer than 1.7 angstrom units (spark gap equivalent of about inch between points of sewing needles). They are capable, however, even in therapeutic doses, of producing superficial atrophy and telangiectases. Absorption is mainly epidermal, so that while telangiectases may occur, sequelae are rarely serious.

The use of soft x rays, produced by a Chaoul tube close to the lesion under treatment, simulates the effect of radium, energy from which falls off rapidly as distance increases. The equipment consists essentially of a shock proof tube, the rays emerging through the 0.. mm. nickel target which serves as anode window and filter in one. By daily treatment a huge total dosage may be built up according to the Coutard plan, and the radiation, originating actually in contact with the tissues that receive it, produces locally typical roentgen destruction.

Bluefarb: APhysTh 5: 400, 1944 (grenz rays).
Bode: DMtsch 75: 313, 193 (contact therapy).
Goin: Radiol 42: 215, 1944 (Philips Metalix apparatus, HVL 0.3 mm. Al, 50 KV, 2 ma).
Hollander and Shelton: ADS 3: 270, 1938 (Chaoul therapy).
Howes and Camiel: AmJR 48: 360, 1942 (contact therapy).
Leitner: BJPhysM 4: 114, 1942 (grenz rays at 12 KV little energy reaches cutis).
Jongman: BJD 61: 151, 1939 (grenz ray therapy of lupus, chronic eczema, Darier's disease).
Pendergrass et al.: Radiol 32: 142, 1939 (Chaoul tube dosimetry).
Ryan: BJD 54: 4, 1942 (grenz rays in acne, herpes, granuloma annulare, neurodermatitis).
Whit: APhysTh 18: 139, 1937 (grenz ray therapy).

**Radium** possesses one great advantage over x rays in that it can be placed in the throat and similar cavities and brought into contact with difficulty accessible diseased tissues. Radium as such does not have any therapeutic value. The tissue reactions which follow radium treatment are the result of the absorption of energy by the tissue from the radiations emitted by radium and its disintegration products, stated Desjardins and

Williams (J 130 207, 1946) whose report by the American Medical Association Council on Physical Medicine is extensively quoted here

Radium is a member of 1 of the 3 radioactive series which occur in nature. The atoms of a radioactive element eventually change into atoms of another element, and this change or disintegration, is produced by the original atom losing mass and energy. The lost mass and energy are in one or more of three forms of radiation called the alpha rays, beta rays, and gamma rays.

"Alpha rays are nuclei of helium atoms which travel at a velocity which may be as high as a tenth of the velocity of light. The emission of an alpha ray by an atom reduces its atomic weight 4 units and its atomic number (number of units of positive charge on the nucleus) 2 units. Although the energy of an alpha ray is quite large, it cannot travel far through solid materials; the greatest distance it can penetrate tissue is about 0.1 mm., and through materials of greater density the distance would be even less. The wall of all the ordinary containers used to hold radium or other radioactive materials is thick enough to stop all the alpha rays.

"Beta rays are electrons which travel at a velocity which may be as high as 99 per cent of the velocity of light. An electron has a mass of approximately one two-thousandth of an atomic unit of mass and has 1 unit of negative electric charge; hence the emission of a beta ray by an atom does not produce any significant change in its atomic weight, but it increases its atomic number 1 unit. The average energy of a beta ray is of the order of a tenth of the energy of alpha rays. Because of their greater velocity, smaller mass and smaller electric charge, beta rays are much more penetrating than alpha rays. Beta rays can travel through tissue a distance of approximately 10 mm. A thickness of metal sufficient to stop all beta rays is often called a beta-ray filter and for the commonly used metals these thicknesses are 0.5 mm. of Pt or Au, 1 mm. of Ag or Pb, or 2 mm. of brass, monel metal, or steel.

"Gamma rays are electromagnetic radiations of shorter wave length than most roentgen rays, ultraviolet light, visible radiations, and radio waves. Like all electromagnetic radiations, they travel at the same velocity as light. The emission of a gamma ray has no effect on the atomic weight or atomic number of an atom. Gamma rays are generally emitted by the same atoms that emit beta rays. In general, the energy of the gamma rays is a little greater than that of beta rays, and they are much more penetrating than either the alpha or beta radiations. One centimeter of tissue reduces the intensity of the gamma rays about 5 per cent, a half inch of lead reduces their intensity about 50 per cent, and some of these rays can be detected through 6 inches or more of lead.

"It is not possible to predict when any particular atom of a radioactive element is going to disintegrate but a definite percentage of the atoms present at the beginning of a period of time will disintegrate during that period. For each radioactive element the rate of disintegration is different and characteristic. Hence the period of time which elapses before half of the atoms disintegrate is called the 'half life period'; this also is characteristic of each radioactive element. The rate of disintegration of an element is not affected by chemical combination, extremes of heat, cold, pressure or vacuum, or by anything which can be done to the element" [excepting by procedures inducing atomic fission]

| ELEMENT | ATOMIC NUMBER | ATOMIC WEIGHT | PHYSICAL STATE | RADIATIONS | HALF-LIFE PERIOD |
|---|---|---|---|---|---|
| Radium | 88 | 226 | Solid | Alpha | 1,590 years |
| Radon | 86 | 222 | Gas | Alpha | 3.83 days |
| Radium A | 84 | 218 | Solid | Alpha | 3.05 minutes |
| Radium B | 82 | 214 | Solid | Beta and gamma | 26.8 minutes |
| Radium C | 83 | 214 | Solid | Beta and gamma | 19.7 minutes |

"If a preparation of pure radium (radium being used as a specific example, although any radioactive element could be used as well) is sealed in a tube, the tube immediately contains other elements. The amounts of these elements will increase for a time, and the amount of radium present will gradually decrease. However, since radium disintegrates slowly the amount present will remain essentially constant for many years and hence the number of atoms of radium disintegrating in any period of time—or which is the same thing, the number of atoms of radon formed in any period of time—will remain essentially constant for many years. The amount of radon present gradually increases until the number of atoms disintegrating in a period of time is just equal to the number of atoms being formed (number of atoms of radium disintegrating) in the same period. From then on, the amount of radon present decreases as the amount of radium present decreases; the ratio of the amounts of all these present is always the same, and radon is then said to be in equilibrium with radium. In a similar manner equilibrium eventually will be established between all succeeding members of the radioactive series. Between radium and radium C, equilibrium is established in about 2 months but it takes only about 4 hours for equilibrium to be established between radon and radium C. The amount of radon in equilibrium with 1 Gm. of radium is called a curie, and smaller amounts are measured in millicuries or microcuries.

Radium is commercially available only in the form of a salt, generally the sulfate, bromide or chloride, and generally a small percentage of the total weight of the preparation is the corresponding barium salt. However the preparation is described as containing a certain weight of radium, which is the actual weight of the radium element present and not the total weight of the preparation. The actual amount of radium present is determined by comparing the amount of gamma radiation emitted

by the preparation (after equilibrium has been established with radium C) with the gamma radiation emitted by a preparation whose radium content is known, or by measuring the rate at which radon is formed. Similarly the amount of radon contained in a tube is generally measured, after equilibrium has been established with radium C, by comparing the gamma ray emission with that from a tube of radium, since the intensity of the gamma radiation from 1 mc. of radon is the same as the intensity of the gamma radiation from 1 mg. of radium, when the two are in equilibrium with radium C. Most commonly the intensity of the gamma radiation is measured with an electroscope or other suitable instrument by determining the amount of ionization produced in a given volume of air.

"Since in ordinary radium treatment only the beta and gamma radiations are used, radium B and radium C are the only elements actually needed because they are the source of these radiations. However they disintegrate rapidly and radium or radon is needed as a constant source for supplying radium B. An applicator containing radium will maintain nearly a constant amount of radium B and radium C for many years, while an applicator containing radon decreases in strength approximately a sixth every twenty-four hours, or a half every 3.82 days, and does not have any therapeutic value after about a month because all the radon and radium B and radium C have disintegrated. Since radon is the only gas in the disintegration series, it can be separated rather easily from the rest of the series, and applicators containing radon are frequently used instead of applicators containing radium. So-called 'radium therapy' may be given with either type of applicator.

"*Treatment with radium can do more harm than good. To determine the best method of applying radium and the amount suitable dose in each case requires training and judgment, and the best results are obtained only by physicians who have had extended experience. For these reasons responsibility for treatment of this kind should be limited to qualified specialists.*

"Ordinary radium therapy can conveniently be divided into three general types of *application*:

I. External Irradiation: the radium applicator is either in contact with the skin or at some distance from the skin. Plaques containing radium, radon bulbs, tubes of radium or radon, and radium bombs are the common types of applicators used for external irradiation.

PLAQUE APPLICATORS usually contain from 5 to 25 mg. of radium embedded in the surface of a glazed material having an area of from 1 to 8 square centimeters. The filter in plaques is very small, seldom more than 0.1 mm. of monel metal; hence most of the beta rays may be used. Plaques are generally placed in contact with the lesion to be treated and are used for surface lesions when irradiation is to be confined to a shallow depth. Although gamma rays also are emitted, their effect on deeper tissue will be slight during the time the beta rays produce a much greater effect on the superficial tissue.

"RADON BULBS are thin-walled bulbs of glass, generally less than a centimeter in diameter containing radon. Since the filtration of the glass wall is very slight, most of the beta rays may be used. Sometimes these bulbs are used instead of radium plaques.

TUBES containing radium or radon generally have walls thick enough to absorb all the beta rays, so that only gamma rays may be used. Walls thicker than a 'beta ray filter' make a mechanically stronger tube but reduce the intensity of the radiation. The [illegible] length (length of [illegible] material) is generally about 1 to 2 cm., the over-all length of the tubes from 1.5 to 3 cm., the outside diameter from 3 to 7 mm., and the wall thickness 0.5 to 2 mm. platinum equivalent (platinum or sufficient thickness of other materials to give a filtering effect equivalent to that of platinum). Often a few millimeters of rubber, bakelite, wood or similar organic filter is used between the tube and the tissue to absorb the secondary radiation from the tubes. Tubes generally contain from 5 to 100 mg. of radium, or up to several hundred millicuries of radon. Tubes are sometimes placed in contact with the skin, but more commonly they are separated a few centimeters from the skin.

"RADIUM BOMBS usually contain from 1 to 10 Gm. of radium, which is enclosed in a large block of lead (or other dense metal) with an opening through which radiation emerges. Filtration is approximately the same as for tubes but the distance between the radium and the skin usually varies from about 10 to 40 cm.

II. Intracavitary Irradiation: the applicators are placed in a natural cavity of the body, usually in order to bring the applicator closer to the lesion to be treated. The most common applicators used are the same radium and radon tubes which are used for external application. The tubes are often enclosed in rubber or similar material to absorb some of the secondary radiation from the tubes and to increase the distance between the tubes and the tissue.

III. Interstitial Irradiation: the applicators are inserted into the tissue to be treated. Radium or radon needles, containing from 1 to 10 mg. of radium or mc. of radon with filtration of from 0.3 to 0.5 mm. of gold or platinum are often used. After the desired dose has been given, the needles are removed. Small tubes containing radon are often used, but these are not removed; they contain such an amount of radon, usually from 0.25 to 2.5 mc., that the desired dose will be delivered while all the radon disintegrates. These are commonly called permanent implants, radon seeds, gold implants or gold seeds and generally are made of pure gold having a filter of 0.3 to 0.5 mm., an outside diameter of from 0.75 to 1.15 and a length of from 3 to 6 mm. They also may be made of platinum.

During recent years in dealing with resistant tumors, the tendency has been to eliminate most or all of the beta rays by using as a filter 0.5 mm. of platinum or an equivalent thickness of some other metal. The reason for this is that beta rays have a decidedly caustic or necrotic effect at short range, that is, on the tissues immediately adjacent to the radioactive substance. This is commonly accompanied by severe pain. Elimination of beta rays by increasing the filtration prevents this necrotic effect and concomitant pain. Less filter is generally employed only to treat superficial lesions.

"The dose of radiation delivered to the tissue—the amount of energy absorbed by the tissue from the radiation—depends on the amount of radium or radon used, the length of time of application, the arrangement of the applicators, the filtration and the

distance between the source and the tissue. The biologic effect produced by irradiation depends on the dose and many other physical and biologic factors, including the rate at which the energy is absorbed, the volume of tissue irradiated and the dosage distribution throughout that volume, the kind of tissue, the phase of the life cycle of the cells, the blood supply and many other factors.

**Dose** is generally expressed in milligram-hours or millicurie-hours, the former being used for radium salts, the latter for radon; the two terms describe practically the same quantity. In ordinary use, however, there will be a slight discrepancy in their values if the change in value of the radon during the time of treatment is not taken into account. If the average value of radon is used, this discrepancy is practically eliminated for any normal period of treatment. To describe a treatment completely, the amount of radium or radon, the time of application, the filtration, the distance from the lesion, and the type of applicator should be given. The roentgen (r) is a measure of the amount of energy absorbed from the radiation; hence it takes into account the amount of radium or radon, time, arrangement, distance and filter. The dosage rate at a distance of 1 cm. from a point source of 1 mg. of radium filtered by 0.5 mm. of platinum, is approximately 8.4 roentgens each hour. When the entire dose is given within a few hours, about 1,000 roentgens of gamma radiation is required to produce an erythema of the skin. Among advanced workers there is an increasing tendency to express radium dosage in roentgens, but at the present time methods of measurement have not yet been perfected and simplified sufficiently to make this a general rule.

**The Maximal Safe Dose** of radiation which a person may receive day after day, called the tolerance dose, is generally considered to be about 0.1 roentgen each day. The dose received by persons working with radioactive materials should be measured by having them carry on their person photographic film or suitable dosage measuring instruments. When the dose which they receive is near or more than the tolerance dose, added protection should be provided. It is advisable also to have frequent studies made of the blood of the personnel, for some of the earliest tissue changes produced by irradiation are indicated by changes in the blood.

**Radon (Emanation).**—There exist 3 series of radioactive elements: the uranium, actinium, and thorium series. Each member of a series is a chemical element. Each differs from the next in the series by either an alpha particle (helium nucleus) or a beta particle (electron). Emanation develops at known rates from each member of the series and can be separated, sealed in tubes, and used separately. The half value period of radon is 3.8 days. A millicurie (mc.) is an amount of radon which will produce the same gamma ray effect as 1 mg. of radium. A gram of radium will produce 166 mc. of radon per day. Tubes containing radon may be implanted in a tumor or applied to the skin surface or used in any way in which radium itself might be used. Histologic changes induced by radon were described by Melnick (PIMChl 13: 84, 1940). Radon ointment can be used (Isaak: ADS 45: 660, 1942; Eldmow: BJD 51: 16, 1939). Dosage was fully discussed by Quimby and Desjardins (J 11.: 1822, 1939).

**Mesothorium** is a radioactive substance in the thorium series. Thorium X bears the same relation to mesothorium that radon bears to radium. Its half value period is 3.64 days. It can be incorporated in ointment or liquid preparations and applied to the skin in the treatment of telangiectasia, eczema, psoriasis, or other conditions (C ro: Lancet 2: 340, 1942.)

**Radium Dosage and Effects.**—Gamma rays of radium are identical, excepting their shorter wave length, with x rays. They have like properties but are highly penetrating. In the use of radium, intensity is greatest at the surface of the applicator which is the source and the analogue of the tungsten target within the x ray tube. Intensity falls rapidly as distance increases from the radium applicator, whereas x ray intensity within the depths of practical concern is comparatively uniform. Thus radium burns are in general smaller in all three dimensions than x ray burns.

The dose with radium or radon is estimated in milligram hours (or millicurie hours) per square centimeter at a given distance with filtration described, or in milligram hours (millicurie hours) per cubic centimeter of tissue when needles or seeds are implanted. Cole and Driver (AmJR 33: 692, 1935) described the interstitial use of platinum needles of 27, 44, and 60 mm. lengths carrying 1, 2, or 3 tubules of radium each 15 mm. long. The over-all diameter of the needles was 1.65 mm., the wall being 0.5 mm., sufficient to filter out all the alpha and most of the beta rays. Such needles will destroy, they found, 1 cc. of squamous-cell carcinoma in 7 days. If placed 1 cm. apart, each cubic centimeter of tissue receives 116 mg. h. of gamma irradiation. They found that failure resulted more often from failure to recognize the dimension of the tumor than from other reasons.

Dangers in the use of radium and radon were elaborated by Cipollaro (J 115 1096, 1940) with whose conservatism we concur.

**Gamma Ray Treatment**, using radium distributed on external applicators and molds, was systematized so as to deliver correct dosage in a practical manner by Paterson and Parker (B J Rad 7: 592-632, 1934). See Meredith et al.: *Radium Dosage: The Manchester System*, Livingstone 1947.

Cutaneous reaction depends to some extent on site, condition and vascularity. For normal skin of face or trunk the expectation is as follows:

- 3,000 r Faint erythema
- 6,000 r Moist desquamation (radio-epidermitis), a reaction which lasts about 6 weeks, after which there is complete return to normal
- ,500 r Severe moist desquamation lasting longer than 6 weeks; the borderline for skin safety

In assessing the response of malignant tissue to radiation it is necessary to assess not the mere surface dose but rather the minimum dose received at any part of the tumor, for this is the only measure of the lethal or sublethal dose. A dose of 6,000 r if delivered to the whole of a tumor and tumor bearing zone causes permanent resolution of the great majority of epitheliomas.

**The Action of Radium Rays** on tumors depends on the kind of cells of which the tumor is chiefly composed. Each variety of cell in the body has a specific range of sensitiveness to the rays, and the sensitiveness of neoplasms correspond closely to that of the normal cells from which the tumor is derived. The sensitiveness of cells appears to depend chiefly on their rate of mitotic activity. Radium rays appear to act mainly on the generative elements of the cells and thus may cause cellular activity to be inhibited, to be completely arrested and the cells to be injured or to disintegrate completely. The rate of these effects varies with each variety of cell and with the age of the cells.

**Radioactive Cobalt** is comparatively cheap and is effective in needles used as radium needles are used (Myers: Sc 107: 620, 1948).

**The Primary Biologic Effect of Irradiation** is one of cell injury. When the degree of injury is small the tissue eventually may be able to recover from it. Hence, in general, it is undesirable to irradiate normal tissue, and one tries to irradiate not more of the normal tissue than necessary while treating a lesion. Precautions must be taken to protect personnel working with radioactive materials from receiving enough radiation to damage them. 0.1 r per day is the maximum allowable.

The action on pathologic lesions of radium rays, like x rays, depends on the sensitiveness of the particular varieties of cells affected. This applies to benign inflammatory and malignant processes. The leucocytes are the most sensitive of all human cells. Young connective tissue cells are comparatively sensitive and mature connective tissue cells are comparatively insensitive to irradiation. Less sensitive or more resistant to the direct action of the rays are cartilage cells, muscle cells, bone cells, fat cells, and finally nerve cells. In the eye the two most sensitive structures are the conjunctiva and the epithelium of the crystalline lens. Doses of radiation insufficient to cause an inflammatory reaction of the eyelids are not likely to cause the conjunctiva or lens to react. Doses sufficient to produce conjunctivitis may lead to the formation of cataract months or years later, especially in children.

**High Frequency and Fulguration Currents** are alternating currents of $10^6$ cycles per second or more, obtained with a spark gap type of generator or a vacuum tube oscillating circuit. High-frequency currents may be applied to the skin by means of vacuum electrodes; the resulting odor of ozone may have good psychotherapeutic effects. Long wave diathermy may be used for heating a large region or concentrated at a point for sur

gical effects in fulguration electrocoagulation, or electrodesiccation. The high frequency caustic spark refers to the local application of a spark by means of an insulated pointed metal electrode effective in destroying small cutaneous growths. **Electrocoagulation** consists in coagulation of diseased areas by means of heat produced at a pointed electrode by a high frequency current. **Endothermy and Desiccation**, the production of heat by resistance of tissues to the passage of a high-frequency current, should not be confused with electrolysis or electrocautery. The applicator is cold when applied and is pointed. It may be employed in either the monopolar or bipolar form. It is an agent for destroying accurately and is used mainly in the treatment of neoplasms. Keloid frequently follows the coagulation removal of small tumors.

**Cautery**—The ordinary electric cautery is simple, reliable, dependable, convenient and economical. With properly designed points, delicate destructive work can be done. By surface application sufficient only to vesiculate, one can destroy leucoplakia and seborrheic keratoses. Its instant effect on cells probably differs little fundamentally from the slower effect of x rays.

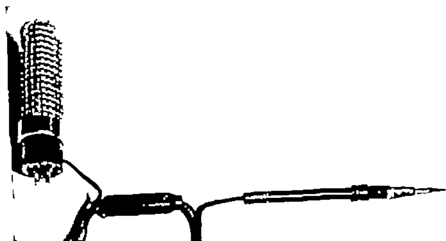


Fig 60—Accurately controlled destruction by intense heat can be accomplished with a cautery of this sort. (Courtesy Post Electric Co Andover N J)

*Electrolysis and Ion Transfer*—When the poles of a galvanic battery contact moist animal tissue, a current passes. Soluble drugs can be introduced into the skin: the positive sponge is moistened with the desired solution, the circuit closed and the current turned on. The procedure is also called iontophoresis, or electrophoresis. See Baker (APhysTh 20 197 1939) histamine and methylcholine Abramson and Gettner (JInvD 4 243 1941) epinephrine Council Rpt. (J 117 360 1941) Pereyra (ADS 52 96 1945) aerosol influence on CuSO penetration Frees (ib 53 34 1946) treatment of tinea and hyperhidrosis by iontophoresis with CuSO

If a needle is used as the negative electrode and is placed within a follicle hydrogen ions accumulate about it and necrotize the follicular epithelium. This agency is used for the destruction of dilated capillaries

and various small growths and is particularly valuable in getting rid of superfluous hairs. The source of current is of no consequence, provided it is direct. A current of 1.0 Ma. is required. Cipollaro (N.Y.S.J.M. 39: 1475, 1939) pointed out the hazards of unskilled use of this surgical ionization and disparaged, as we do, the multiple needle technic.

Some operators use the high frequency current applied through the electrolysis needle for a brief instant in contrast with the 10 to 20 seconds required by the galvanic current. Great skill is required to prevent scarring (Karp: ADS 43: 85, 1941; Erdos-Brown: ib. 46: 496, 1942).

**Heat (Hyperpyrexia)** as a therapeutic agent has been recognized during many centuries of medical activity. In recent times novel measures for producing and maintaining heat have been developed. More kinds of dermatitis are soothed by cool applications than by hot ones. Fever is thought to be a protective physiologic response although the nature of it is not understood. Since some parasites are killed or damaged by temperatures that human tissues may be able to tolerate, artificial fever therapy has a rational basis. Its status practically must depend on experiment. The means for producing fever is of no matter in itself it is generally thought. Methods of producing fever include baths, cabinets with electric lights in them, electric blankets, medical diathermy machines, induction machines, foreign protein and malaria. Short wave radiation was found to provide simply comfortable warmth for the cultivation of many bacteria when Liebesny et al. (Klin.Wchr. 12: 141, 1933) tested its effects. There is always danger of burns, exhaustion, heat stroke or cardiovascular accident whatever the means used, and it should be borne in mind that a cure ought not to be more severe than a disease. Real utility of heat treatment has been demonstrated in syphilis (see p. 267) and gonorrhea (Tauber and Goldman: ADS 41: 917, 1940; Krusen and Elkins: J. 112: 1689, 1939). Atopic eczema may respond favorably temporarily.

Heat usually relaxes muscles, increases the transudation and rate of lymph drainage and the removal of subcutaneous d..., promotes vasodilatation so increasing the rate of blood flow and induces temporary leucocytosis. Infrared treatment should last at least 30 minutes and cause erythema. Such radiant or incandescent heat is more penetrating than nonluminous energy which feels hot but penetrates only a millimeter. Conducted heat is least penetrant. It may be obtained with water bottles, baths, pads, blankets or the paraffin bath which last we have found useless in dermatology.

# DERMATOSES DUE TO PHYSICAL AGENTS

## TRAUMATIC DERMATOSES

The skin is subject to injury by pressure friction, abrasion, ex coriation bruises, tearing cuts, splinters, and the like. Xerotic skins have a relatively thin epidermal layer vulnerable to alkali. The ease with which sufferers from epidermolysis bullosa or cutis hyperelastica are in jured comprises a significant feature of these diseases. Hair and nails may be traumatized. Permanent wave devices may pull a wisp so that parts of the scalp become sore and even temporarily denuded. A long toe-nail in a short shoe may be blistered loose in walking

**Friction Dermatitis** occurs in occupation where the exact method of performing the job must be understood in order to clarify diagnosis and correctional effort (Tulipan and Appel MRec 154 443 1941) Oc cupational corns, calluses, and stigmas are of this nature (Ronchese J 128 925 1945) *Occupational Marks and Other Physical Signs* Grune & Stratton, 1948) Injury by silicous spicules from certain sponges handled by oystermen (Corson and Pratt ADS 47 574 1943) and asbestos corns (Howell and Alden ADS 49 312, 1944) exemplify possibilities. Shaving especially shaving against the grain, may provoke troublesome me-chanical irritation of the face (Baer UCutRev 45 446 1941) and beard hairs falling onto the skin from an electric razor were reported as be having like itch powder (Moore ADS 44: 69 1941) Clothing is a common cause wool or starch being the usual offender In infants the neck flexures and medial aspects of the thighs suffer from snowsuits. Chafing if severe, disrupts the epidermis sufficiently so that oozing and crusting occur and secondary infection may complicate the situation

Patch tests, as Tulipan and Appel pointed out are not likely to be helpful, for they do not reproduce the mechanics of etiology Efforts to cure such eczema by diet are even farther afield. Petrolatum allevi-ates, but cure requires elimination of the cause.

**Abrasions and Excoriations** are recognized by linear discrete lesions where superficial layers of skin have been scraped away Protection and the prevention of secondary infection suffice in therapy After careful, thorough cleansing, a dressing of petroleum jelly comforts a floor burn and allows it to heal.

**Bruises** are colorful because blood has entered the skin from broken vessels. If the accumulation of blood beneath the skin is large (ecchy moma) it may require evacuation, although resorption if infection does not occur is usually complete. If not complete, organization of the clot takes place with a cicatricial result such as cauliflower ears.

**Wounds** of the skin require cleansing of edges, hemostasis, neat apposition, and a protective dressing. Scalp wounds rarely become in-fected. Débridement may be necessary if a crushing injury of the skin is untidy To minimize the scar of an elliptical excision held together by a few skin sutures, the sutures may be removed after 24 to 48 hours, ap-plying Scotch tape over the wound to support it for the next few days.

**Splinters** are often best removed by attacking the deep end and work ing toward the point of entry

## CORN

**Symptoms** — A corn is a circumscribed slightly elevated hypertrophy of the horny layer cone-shaped with the apex pointing inward. Corns occur on the toes or other places exposed to friction and pressure. Generally smaller and more sharply circumscribed than calluses, a corn is distinguished by the presence of a horny core or tap the deep end of which presses on the tender cutis. Hard corns occur on exposed surfaces, and their tops are rounded and burnished. Soft corns develop between the toes and as a result of maceration and mycotic fermentation are soft, moist and grayish. Following infection with pyogenic organisms, either type may suppurate with more or less resultant ulceration. Corns arise as the result of pressure or friction usually from ill fitting shoes. Orthopedic disorders often play an important role. Some occupations cause corns to develop.



Fig 51.—Corn



Fig 52.—Callus. (Dr Sam Sweitzer)



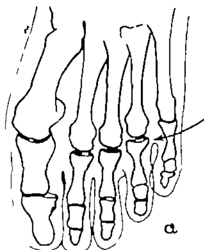



Fig 53.—Soft corn, due to pressure of bony spur on proximal end of proximal phalanx of fourth toe (Mace. J.A.M.A. 115 [illegible] 1940.)

**Seed Corns** are circumscribed plantar dyskeratoses which can be picked out, only to recur. They are not traumatic corns, verrucae, or senile keratoses, or punctate keratoderma but perhaps are volar seborrheic keratoses.

**Treatment.**—The basis of successful treatment is to remove the cause. The adoption of broad toed, foot form shoes made of soft leather will often prove curative Orthopedic consultation and correction may be required. The lesions can be removed temporarily by the use of 40 per cent salicylic acid plaster A chisellike instrument is especially adapted to the trimming of corns, after which the cavity is painted with tincture of iodine. (Ellar AmJS 29 444 1935 )

## CALLUS

**Symptoms.**—A callus is a hyperkeratotic plaque due to chronic intermittent pressure and friction. The sites of predilection are the volar surfaces. The lesions are yellowish or brownish with slightly elevated, burnished surfaces. At the circumference they merge into normal skin Often occupationally determined, they are seen on the hands of mechanics, blacksmiths, metal workers, leather buffers, stokers, and oarsmen, on the fingers of harp and violin players, and even on the lips of trumpeters. They do not arise spontaneously Differentiate keratoderma climactericum (q v )

**Treatment.**—The lesions are likely to undergo fissuring which is painful. They can be temporarily removed by applications of 20 per cent salicylic acid in an ointment vehicle or by careful shaving Permanent relief can be secured only by removal of the cause, which may require orthopedic consultation.

## SCAR

**Symptoms.**—Cicatrices consist of new connective tissue which replaces mesodermal discontinuities caused by trauma or disease. They are whitish or pinkish in color and firm in consistency Their outline approximates that of the lesions in which they develop Their surface may be depressed below the level of the surrounding skin, atrophic scars the surface may be on the plane of the skin or it may be elevated, hypertrophic scars Neatest cicatrices are those resulting from clean incised wounds when the edges have been held together In variola, syphilis, and herpes zoster the lesions are atrophic white and soft Hypertrophic scars develop as a rule from burns and following deep lacerated or infected wounds. They never extend beyond the boundaries of the original injury a feature which distinguishes them from keloid Symptoms are commonly absent. If present they are usually burning prickling or formicating in character and result from nerve filaments caught in tiny amputation neuromas (Kredel Surg. 8 98, 1940) Scars tend to contract, *mainly in the diameter perpendicular to the lines of cleavage.*

**Treatment.**—Irregular or hypertrophic disfiguring scars can sometimes be excised. The surface can be rendered smoother and less conspicuous by the use of solid carbon dioxide, x rays or radium. Blistering doses of ultraviolet irradiation diminish the conspicuousness of shallow scars, it is thought see treatment of acne.

## THERMAL INJURIES

**Erythema.**—The initial stage of inflammation is manifested by capillary dilation, clinically visible as redness, or erythema. The color is blanched by pressure. If the cause of hyperemia acts over a period of time, or with considerable intensity exudative changes occur Hyperemia

may be active or passive the former being inflammatory erythema, the latter representing venous stasis. Erythema may be due to the action of external agencies such as heat cold and traumatic and chemical irritants (erythema venenatum) Symptomatic erythema develops as a result of some internal or systemic cause affecting vessel walls or their nerves. Cutaneous vasodilation is erythema which may exist as a temporary phenomenon of vascular activity such as blushing or as a permanent change in the vessels, such as port wine angiomas.



Fig 54.—Old scar of burn



Fig 55



Fig. 56.

Fig 55.—Erythema ab igne marmoraceous appearance induced by hot pad.
Fig 56.—Frostbite showing resultant telangiectasia. (Dr Stuart W y)

Erythema is recognized by pressing upon the lesion the color fades but returns promptly on releasing the pressure. A petechia is not blanched by pressure. The cause of the erythema may be indicated by its location, distribution, duration and history in the light of knowledge of possible causes.

**Erythema Caloricum** and **Erythema Pernio (Chilblains)** are erythemas due respectively to heat and cold. The effects of radiant heat such as the long-continued applicaiton of an electric pad, produce erythema ab igne. In this condition, there is often accompanying inflammation, and pigmentation is usual. Chilblains are purplish infiltrated lesions which develop on the nose ears, heels, and other prominences as a result of repeated exposure to cold. They are common in damp cold climates, such as that of London, and occur especially in persons who habitually suffer from cold hands and feet and who are said to have chilblain circulation Marmoraceous redness of the arms and legs, more pronounced on the dorsal surfaces, is notable in many persons, especially those who are long accustomed to being not warm enough. The skin is cool and puffy and it may become hypertrophic to a degree that justifies sympathectomy which results in vasodilation warmth, and relief See pernio p 69

**Burns** range in extent and severity from slight localized redness to widespread tissue necrosis. They may be divided according to severity (1) burns of first degree, characterized by the presence of the inflammatory signs of heat, pain, redness, and swelling, due to necrobiosis of epithelium and superficial vessels (2) burns of second degree characterized by these symptoms, plus vesiculation and exudation due to epithelial necrosis (3) burns of third degree, including all thermic injuries of the skin which result in necrosis of both epithelial and connective tissue substance. Primary shock in extensive burns is like other surgical shock, and is to be treated with plasma, blood transfusion, dextrose, oxygen, sedation, heat, and perhaps adrenal cortex extract (Harkins J 119 385, 1942) In burns that destroy nerve endings, pain may be wanting but shock appears in a few hours In severe burns the patient should be treated for shock at once whether he shows it or not. Aldrich (NEngJM 217 911, 1937) stated that delayed shock, which comes on after from 10 to 20 hours, attributed to histamine by others, is simply inadequately treated primary shock the viscosity of the blood is increased even more in capillaries than in veins, and the patient develops red blood-cell emboli which cause fatal anuria, ulcerative colitis, and focal necrosis of adrenals, lymphoid tissue, heart muscle and other organs. Intoxication which comes on still later Aldrich thought to be bacterial intoxication although this is open to question (McClure J 113 1808 1939) It may be prevented by maintaining bacteriostasis of damaged areas. Pyemia, erysipelas, and tetanus are among the complications one anxiously avoids. When vibrissae are burned, look out for laryngeal and tracheal involvement, and include high humidity in therapy When nails are blistered off digits are usually lost.

**Cosmeticians Burns.**—Deep little burns are often caused by inept use of permanent wave machines. Severe burns can result from ignition of celluloid combs.

**Phosphorus Burns** are extremely pai ful and slow to heal because of the formation f $P_2O_5$, wh ch combines with tissue fluid to make phosphoric acid Emergency treatment requires immersion i water or wrapping with wet blankets to smother the fire later picking out bit of phosphoru while swabbing with warm 3 pe cent solution of sodium bicarbonate Copper oleat prepared from the sulfat mixed with soft soap, inactivates by combining with phosph rus t form coppe phosphide (McCarthy nd Pettt BMJ 2: 316 1943)

**Hydrofluoric Acid Burns** are comparatively painless for several hours despite deepening ecrosis. They re best treated by applications of sodium bica bonate solution and magnesium oxid paste injecting under them 10 per cent calcium gluconat to stop thei progress (Jones JIndustHyg 1 203 1939)

***Prognosis.***—*Of 1,674 burns, death was the result in 8.2 per cent of* those due to scalds, 31.2 per cent of those due to ignition of clothing and none in those due to contact with flames or hot solid bodies (Lutken Ugesk. f Laeger 20 409 1937) The outlook depends on promptness and effectiveness of treatment as well as extent of injury Of 250 burned children, all who lived to the tenth day survived 14 deaths occurred pneumonia topping the list of contributory causes (Lavender J 118 344 1942) Among 6 000 deaths reviewed by McClure (J 113 1808, 1939) almost half involved children under 6 years of age and four fifths of these were preventable Loss of plasma protein was important also tissue anoxia due to hemoconcentration and circulatory failure Liver cell damage perhaps due to absorption of toxin formed in the burn was conspicuous. The possibility of recovery is to some extent inversely proportional to the area of the burn. Berkow (ASurg 8 138 1934) estimated the area in adults, of head 6 per cent upper extremities 18 per cent trunk including genitals 38 per cent, and lower extremities 38 per cent. Of the lower extremities, the feet comprise one sixth, the legs one-third and the thighs one half In children under 12 years, the head is larger and the lower extremities smaller Burns exceeding 50 per cent of the surface are extremely grave.

If metabolic demands of the tissues are met shock adequately treated, hemoconcentration corrected (hematocrit kept under 55) rigid asepsis maintained, and toxicity successfully combated the outlook is favorable (Pemberthy and Weller SGO 74 428 1942)

Intravenous injection of fluorescein sodium 10 c c. of 20 per cent solution followed by illumination in ultraviolet light distinguishes second degree burns which glow yellow from third degree burns which look purple or black (Dingwall and Andrus AnnSurg 120 377 1944)

**Treatment.**—In severe cases, supportive treatment is essential. Blood plasma transfusions are useful (Elman J 116 213 1941) as well as oxygen inhalations. In small burns soothing and protective lotions, such as cool moist packs and petrolatum are all that is needed. In burns of second degree the vesicles should be incised and drained aseptically loose epithelium removed, and an antiseptic dressing applied Aqueous solution of gentian violet or some other dye may be employed. Butesin picrate is unsatisfactory because eczematous reaction to it is common.

Under some circumstances, the entire burned area should be excised. A patient may be placed under a cradle with electric lights as the source of radiant heat and the entire area is covered with sterile gauze kept wet with hypertonic saline.

For extensive burns, Davidson (SGO 41 202, 1925) recommended aqueous solution of tannic acid applied by spray Coagulants other than tannic acid can be used. Dyes, such as gentian violet, are useful, but Cohen (BMJ 2 251 1940) found in war experience that tannic acid and silver nitrate are preferable. The eschar produced by tannic acid is inflexible and tends to curl at the edges, and infection cannot readily be detected beneath it Septic toxemia is more likely to occur in deep burns, and may have its onset after 7 days. Bland, wet dressings and ointments are much to be preferred in small second degree burns. Blisters open 24 hours before tannic acid is available are already infected and should not be so treated. Burns of hands and fingers should be treated with a grease, not with tannic acid (MacCollum J 116 2371 1941) Tan

nic acid is nowadays assessed as doing more harm than good, though it relieves pain; infection spreads under the eschar and intoxication with liver damage occurs (Lee and Rhoads J 125 610 1944)

Asepsis requires masking and education of personnel who handle burned patients as well as proper bandaging and strict attention to detail (Colebrook et al. abs J 128 907 1945) Azotemia occurs early and usually is reversible as urinary output approaches normal, but in some severe cases it does not disappear Hypoproteinemia and inversion of the A/G ratio must be watched for and are met by increasing alimentation (Taylor et al. NEngJM 229 855 1943)

Swelling, which accounts for great loss of protein and fluid into the interstitial spaces, may be controlled with pressure bandages or even plaster casts (Levenson and Lund J 123 272, 1943 Harkins ib 125 533 1944)

Paraffin wax depending for antisepsis on sulfanilamide (Pendleton J 122 414 1943) or penicillin and propamidine cream may be applied (Clark et al. Lancet 1 605 1943) Continuous bath treatment was described by Lavender (AmJSurg 45 534 1939) Continuous irrigation of the burned part within an enveloping bag was recommended by Pearson et al. (BMJ 2 41, 1941) Pyruvic acid in 8 per cent cornstarch paste at pH 1 9 is said to clean sloughs in 4 days so that grafts can be applied early (Connor and Harvey AnnSurg 120 362, 1944) Flash burns from explosions may be serious and are common in war a protective cream has value (BullUSAMD 76 7 1944)

**Frostbite** produces reddish or violaceous localized plaques on the hands and feet and occasionally on the face or ears, known as chilblains, or perniones. These lesions may be persistent, giving rise to smarting and itching especially when the part becomes warm Severe frostbites corresponds to burns of the second and even third degrees. Vesicles and bullae develop and gangrene may result. Necrosis may involve only the skin and subcutaneous tissue or it may include a whole extremity (Greene Lancet 1 303 1940)

**Pernio.**—The pernio syndrome may include the acute form of chilblains, the chronic form of chilblains, and perhaps immersion foot or trench foot. According to Allen et al (*Peripheral Vascular Diseases* Saunders, 1946) it seems that a similar mechanism operates in all these conditions and has as its outstanding feature a reaction of the peripheral blood vessels to cold. Clinical features are similar and such differences as occur in the nature and extent of the symptoms and signs are due to differences in severity length of exposure and variability of vessel response to cold.

**Acute Pernio** is experienced by a child who goes out in the snow or cold wet weather without adequate protection for feet and legs, and develops dermatitis characterized by a bluish red color and the slight edema in the affected regions. Intense itching and burning are aggravated by exposure to warmth. The manifestation exists for several days but gradually fades. Sometimes brown pigmentation persists for several weeks. Rarely purpura develops in the affected region during the acute stage.

**Chronic Pernio** is seen in susceptible persons who have been repeatedly exposed to cold and in whom develop recurring and chronic cutaneous lesions, which are erythematous, ulcerative and hemorrhagic and which often leave residual scarring, fibrosis, and trophic [illegible] of the skin and subcutaneous tissues after healing. The lesion usually are active during the cooler months and may subside completely during the warm season, when the diagnosis is obscure because the etiologic significance of cold is overlooked. Such cases have been called erythrocyanosis, Bazin's disease, dermatitis hiemalis, and lupus pernio. Confusion has resulted, according [illegible]

et al. (*Peripheral Vascular Diseases*, Saunders, 1946) from failure t distinguish this syndrome from tuberculous erythema induratum (q.v.) from which it is differentiated by histologic examination.

The lesion are of various sizes, elevated and horseshoe shaped, reddish or slightly cyanotic perhaps vesicul tel r ulcerated On healing, atrophic violaceous scars develop. Hist logi hanges comprise (1) angiiti with intimal proliferation, thickening of the arterial wall and periarterial and perivenous infiltration of lymphocytes, monocytes a l neutrophils, ( ) necrosis of the fat panniculus, and (3) hronic inflammatory reaction of th subcutaneous tissues in which giant cells may be found.

The typical patient with chronic pernio a described by Allen et al. (1946), is a woman who complains of recurring erythematous, and ulcerating lesion f the lower extremities. These made thei appearance in adolescence or early adult life and at first appeared at the onset of cold weather and disappeared during the summer On exposure to col l burning and it hing sensations developed i the affected regions, the lower part of the legs. Red, slightly elevated lesions from mat khead t dime size appeared over the anterior and posterior leg region f involvement and sometimes on the dorsum f the feet and on the toes. Blisters developed on these and the color f the lesion deepened in it violet hue Superficial ulceration ensued with a hemorrhagic yanotic base but with little exudation. Pain was at first present but later subsided. Healing eventuated within three t five week spontaneously and pigmentary residuals persisted. When new rops of lesions appeared, the procedure wa repeated. In such cases crops may appear over a period f several months. During the active stage the lower extremities are cool and slightly yanotic in a cool environment The legs may be somewhat edematous. Livedo reticulari may be present. The peripheral arteries pulsat Evidences f occlusive arterial d ease are absent

FROST INJURIES IN WARFARE were well described by Lieberny (NYSJM 44 115, 1944) who li ted types erythema and edema, blisters, superficial gangrene gangrene f k n and subcutaneous tissues, gangrene f an entire acral part injuries to deep ti sues w th or without accompanying skin lesion and hronic relapsing cutaneous ma fest tion such as hilbl ins and other form of erythrocyanosis Light freezing provokes onl local redness, while exposure to temperature f 10 to 20 F for 20 second is followed by t hing and wheeling typical f response t acute physical injury subsiding a a few hours, w th local tenderness for a week and some peeling (Lew BMJ 793 869 1941) More severe injury causes blistering within a hou or two, which can be predicted f t hing and burning pain accompany the period f thaw ng Frostbite at h gh alt tude depend in part on v sospasm and noxemia f r fi gers are more susceptible than cheeks (Davis et al. ROO 561 1943) Arteriolar damage b y lott ng due t agglut nat on f red cell can be prevented by hepari (Lange et al. NEngJM 3 393 1947; ROO 82 36, 1946)

IMMERSION FOOT (TRENCH FOOT) occurs when the feet are long exposed to cold and wet ess This may develop even when th temperature is above freezing Dilat on a d engorgement of vessel of k n and sube t eous tissues occu along w th aggl t nati e thrombi composed of red cell and platelet (B HUSAND F b, 1943) Numbness accompanied b y swell ng and waxy wh teness w th scatt red yanoti spots. Swell g increases rapidly whe th part are warmed, whe redness, hyperem a, bounding pulse within the parts, a d tense pa n experience. Depending se erity f jury blebs which may be bloody nd ulceration develop t sues m t ra bla k a d dry r mo st ga gre e becomes ma fest (Gree e La et l 303 1940 W bst et al. JBJSurg 4 693 194 ) Recovery may be complete or chronic neuralgic pa n may begin or h perhidrosis with soggy fragility f the epidermis may be sequel, along with hypesthesia.

Control requ res proper equ pment avoidance of risk, enforced foot hygiene with cleanliness dryness, warmth and frequent inspect on.

Treatment requires rest elevation cold applications d ring the early phase to relieve pa and a o dance f trauma nd feet on Heparinization if accomplished within 48 hours l continued f 7 t 9 days while the part are kept at room temperature prevent ga grene (Lange et al. NEngJM 237 393 1947) Some 300 mg of heparin in 5 l t rs f sal ne solut on are given intra enously daily t a rate of 20 t 25 drops per minut testing the lott g t me e h l hours and maintaining it between 30 and 60 tes

Late sequela re fairly common, including chronic peripheral vascula disease subjective cold ess d plantar schemia (Fausel and Hemphill ROO 81 60 1945) Sympathectomy ma then be d isable (White NEngJM 228 11 1943) The indications for sympathectomy ccordi g to Shumacker and Abramson (AnnSurg 123 203,

104 ) who reviewed the effects of the measure as performed on 49 of 700 Mayo Clinic patients, include extensive gangrene excessive sympathetic tonus, and pain on weight bearing It is not appropriate in the majority of cases.

Chilblains may respond well to nicotinic a id in doses not exceeding 300 mg per day (Gourlay BMJ 1: 336, 1948)

Livedo Reticularis is characterized by a local and prominent mottling and blotchy or reticular discoloration f the skin of the extremities, of reddish blue color Williams and Goodman (J 85: 933 1925) divided cases into three groups: (1) cutis marmorata, manifested by mottling of the skin on exposure to cold with disappearance on warming (2) livedo reticularis, idiopathic with bluish-red mottling more intense than in cutis marmorata and persisting in spite of temperature changes; and (3) livedo reticularis symptomatica, in which mottling persists but evidence of some other disease is also present, affecting the cutaneous vascular system.

Erythrocyanosis (Acrocyanosis).—Almost constant coldness and bluish discoloration of the fingers and hands for many years are the features of acrocyanosis. The same changes may occur in toes and feet to a less degree. These changes, while more intense in cold weather persist in a warm environment. The color is deep purple when the skin is cold and red when it is warmer Scleroderma does not develop, but swelling and puffiness occur particularly in cold weather and some areas may become painful. Atrophy or ulceration does not take place. No evidence of occlusive arterial disease is to be found. Acrocyanosis i distinguished from Raynaud s disease by the persistency of ts color change and the absence of pallor In erythromelalgia the region of color change is hotter than normal, while in acrocyanosis such regions are cool. Cyanosis in the presence of occlusive arterial disease is related to ischemia and is not true acrocyanosis.

A bluish-red network involves generally the legs, being supramalleolar in distribution, and the forearms; it is greatly intensified by exposure to cold or friction. Only a small drop in temperature suffices to bring on the appearance of vermilio spots which accompany purplish infiltrates. The causative mechanism probably is partial obstruction f arterial supply due to cold sensitivity for nerve block temporarily relieves th condit on. It is likely that vasomotor instability of psychosomatic origin plays a part in causation, for cold, moist hands and feet, with dependent cyanosis characterize the sufferers from this disease In therapy continued warmth, such as that provided by ce tral heati g, is helpful. (Ebert. ADS 16 426, 1927; Clouston CanadMAJ 40 166, 1939; Lewis BMJ 2 837 1941; Wrong CanadMAJ 48 520 1943 Barker et al. AmHJ 21 592, 1941.)

## ACTINIC INJURIES

**Sunburn** is a common simple erythema (see p 65) Persons differ in their susceptibility blonds being especially sensitive. Erythema limited to the exposed areas has its onset within a few hours after exposure begins, the interval depending on susceptibility and dosage. Vesiculation is characteristic of severe exposure, and extreme cases are sometimes seen. If a large area is involved, in addition to pain, smarting burning and swelling there may be severe constitutional symptoms, including weakness or collapse, fever chills, and even delirium. Secondary infection may complicate the condition. Maximum intensity is reached within 12 to 24 hours after exposure and recession of signs and symptoms then begins. Peeling follows and is accompanied by itching More or less temporary pigmentation ensues. Increased tolerance of sunshine is gained when estrogenic hormone is taken (Lancaster SMJ 32 395, 1939) The electric arc in welding provokes actinic conjunctivitis (Rieke J 122 734 1943) but glasses, clear or tinted, protect the eyes from ultraviolet energy (Blum WarM 4 388, 1943)

Physiologic Effects of Ultraviolet Light.—Antirachitic action takes place in th lowermost h rn cells. Erythema results from action in the basal layer of the ep dermi and the superficial portion of the corium. The basal epidermal cells are st mulated, nd increased amounts of the products of their activity are set free; it is these substances which result in local hyperemia nd which act also on distant

parts of the body when absorbed and transported. Ultraviolet light produces maximum burning effect at a wave length of 2,967 A.U. The longest wave capable of burning is at 3,130 A.U. Too intense a tion kills the basal cells of the epidermis so that ultraviolet irradiation is shock treatment and its dose depend on the individual's reaction to it. Care should be used to avoid overexposure. Not only may painful sunburn result but more deep-seated injury may occur as indicated by nervousness, apprehensiveness, and insomnia. (Laurens: J 111: 393 1939)

**Treatment.**—A soothing, cooling protective mixture like calamine lotion is beneficial, or modified zinc oil may be prescribed:

| | | |
|---|---|---|
| ℞ | Phenol | 0.3 |
| | Menthol | 0.06 |
| | Zinc oxide ointment | |
| | Wool fat | 15.0 |
| | Limewater to saturation | |
| Sig.: | Soothing liniment | |

Sunburn is best alleviated by wrapping the parts with soft towels moistened with aluminum acetate solution gr. xv to the pint of water. The patient must be kept warm if extensive wet packs are necessary. Vesicles should be incised, and per cent aqueous solution of gentian violet is valuable in combating or preventing infection. Later a bland greasy preparation, such as Posey's liniment, is comforting. A good preventive is 2 drams of zinc oxide in an ounce of aquaphore. Phenyl salicylate (salol) 10 per cent in liquid petrolatum and stearates are also efficient in protecting the skin. (Sharlit: ADS 3: 200 1933. Strakosch: JInvD 5: 1 194-) A protective lotion may be prescribed of skin tint: red ferrous oxide 1.0, yellow ferrous oxide 1.3, titanium dioxide 13, bentonite 3, rose water to 100. Dark red vet. petrolatum is effectively opaque (Luckiesh et al. J 130: 1 1946). Para-aminobenzoic acid, 15 per cent in Kessler's cream, protects against rays of 2,900 to 3,100 A.U. (Rothman and Henningsen: JInvD 9: 307 1947). Pyribenzamine inhibits sunburn because the absorption curve of the chemical has a high extinction peak in the erythemogenous part of the spectrum (Kline and Baer: JInvD 10: 307 1948).

## X RAY AND RADIUM INJURIES OF THE SKIN

The influence of x rays and radium is necrobiotic (see p. 65). Some kinds of cells are more susceptible than others to this effect which is proportional to the quantity of x ray energy absorbed. Judicious use may be made of this phenomenon; unfortunate results are x ray burns and dermatitis.

**Symptoms.**—Gilchrist (BullJHH 8: 17 46 1897) recognized the specific skin disease caused by x rays. The reaction following overexposure to x rays varies in degree: erythema, vesiculation, or even gangrene may result. *The reaction appears after from 2 to 10 days.* In mild acute reactions, the redness which is accompanied by tenderness, burning and itching disappears within two or three weeks, leaving temporary pigmentation such as follows sunburn. There may be periodic recrudescences of erythema which rapidly diminish in intensity but are observable for several weeks. In chronic cases which result from excessive employment of doses which if taken singly would not give rise to erythema, the skin becomes thin, dry, atrophic, wrinkled, telangiectatic, and pigmented. Keratoses may develop and some of these may become carcinomatous. Nails become thinned, striated, and brittle. In severe burns marked dermatitis develops with vesiculation followed by more or less necrosis. Ulcers thus formed are covered with thick, tough, adherent, brownish or grayish membranes and are exceedingly painful. They heal slowly if at all. Radium burns are similar but are smaller in all three dimensions.

The most common cause of x ray burns is failure to insert filters when the treatment planned includes their use (Saunders and Montgomery

J 110 23 1938) Mistaken diagnosis, inadequate records of previous radiotherapy, improper calibration, faulty fluoroscopic technic, unwise therapy in diseases for which x ray is only palliative, and stupid disrespect for or ignorance of the harmful potentialities of exposure are other causes (Leddy and Rigos AmJR 45 696 1941 Garland J 129 419 1945)

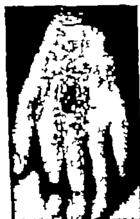


Fig 57



Fig 58

Fig. 57.—Chronic x ray dermatitis and ulcer

Fig. 58.—X ray atrophy and carcinomas from mistreatment of pruritus ani.



Fig. 59.—Chronic x-ray dermatitis atrophy of epidermis, dilation of vessels, advanced degeneration of collagenous tissue, absence of appendages. (Dr George M Mackee, from McCarthy *Histopathology of Skin Diseases* The C. V Mosby Co.)

**Atomic Energy Injuries** resulting from the explosions of atomic bombs in Japan were reported by Keller (J 131 504 1946) and Timmes (USNMBull 46: 219 1946) Radiation sickness, damage to the hemato-

poietic system and x ray injuries of all sorts occurred The scars of the flash burns, due to actinic energy did not produce an unusual proportion of keloidal reactions, thought Warren (MilSurg 102 93 1948)

**Pathology**—Early there is edema of the epidermal cells, followed by degeneration of nuclei Vascular endothelium is similarly affected. Severe doses cause necrosis, hemorrhages, and obliteration of small vessels Fibrous tissue nuclei swell and fragment and collagenous tissue takes a mucoid appearing stain. The epidermis becomes flat and atrophic and appendages are lost (Harvey EdinMJ 49 529 1942.)

**Treatment.**—In severe cases, excision, followed if necessary by grafts, may be necessary Pain is relieved at once Aloe vera, a gelatinous material applied as a poultice and effective largely because of its physical properties, has been favorably reported by Loveman (ADS 36 838, 1937) In mild roentgen dermatitis, astringent soothing lotions, such as aluminum acetate alleviate Boric acid ointment with 0.5 per cent phenol or Aquaphor is a suitable bland protective tetracaine 0.5 to 1 0 per cent may be added. Sellers (JMichSMS 41 59 1942) recommended Theelin in oil, 10 000 units per cubic centimeter locally Late cases may be helped by superficial desiccation (Cannon NYSJM 40 391 1940) or major surgical effort may be required (Bevan SClinNAm 1 935 1921 Ghormley and Fairchild Surg 7 737 1940) Chronic ulceration in postirradiation scars responded favorably to weekly infiltration with about 0 5 c c of penicillin 50 000 units per cubic centimeter into each 1 c.c of affected tissue after preliminary infiltration with 1 per cent procaine reported Lamb and Boyer (HawD 11 3 1948) Ulceration may be due to low grade infection

# DERMATOSES DUE TO CHEMICAL AGENTS

## DERMATITIS FROM DEFATTING

Solvents and surface active agents, including soaps, abstract oil from the skin. Frequent subjection of the integument to them results in damage which is chemical in origin but is not a sensitivity phenomenon. Individuals vary in their susceptibility to this abnutzung dermatitis, the red haired and xerotic patient being especially vulnerable. Disease is more likely to occur during winter months when artificially heated air is of low humidity and sebaceous secretion is at its seasonal minimum.

Like dermatitis caused by primary irritants, defatting may damage any skin. The hands are the usual site and occupation such as that of the housewife, is a predisposing etiologic factor. Soap takes out oil more effectively when used with hot water and the girl with chapped hands will accept good advice when one explains, "You can't wash dishes free from grease with cold water."

Manifestations of dermatitis from defatting include dryness and inflexibility of the skin especially over the knuckles, hyperkeratosis, often with some scaling and perhaps fissuring. Treatment promptly relieves if contact with the defatting agent is sufficiently reduced and the skin is lubricated with hydrous wool fat or an equivalent oily substance.

## CONTACT DERMATITIS

**Symptoms.**—Dermatitis venenata (contact dermatitis, eczematous or allergic dermatitis) is dermatitis due to cutaneous reaction to chemical substances when they have touched the skin. All degrees of inflammation from simple hyperemia to gangrene may be encountered. Most cases are at first itchy, then erythematous, and are limited to the regions touched by the irritant. Later they become papular and vesicular and pustular if secondarily infected. The lesion may spread beyond the borders of the zone of original contact, and widespreading manifestations may appear scattered over the body depending on conveyance via fingers or clothing and on the degree of cutaneous reactivity to the contactant.

The eruption which results from a single contact with the offending substance is self limited. It disappears spontaneously within a few days or weeks. Repetitions of contact are often the case however. The response of the sensitive skin may become progressively more intense with spread of reaction far beyond the original site.

The clinical picture and the history that the patient gives intimately depend on the time intervals involved: daily association with a deleterious agent evokes continuous and chronic disease, while occasional flares result from and denote corresponding occasional contacts. Thus investigation of etiology in a given case requires intelligent questioning of the patient, for periods of freedom from disease are as significant as periods of activity.

Continuous or frequently repeated exposure results in disease which reaches maximum intensity and remains either unchanging or spreads in



Fig 60

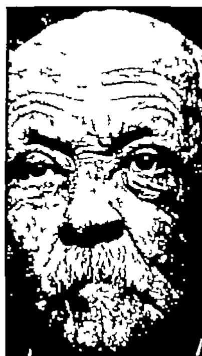


Fig 61.

Fig 60 —Dermatitis [illegible]enenata, [illegible] t (Dr J F Gaequierre)

Fig. 61 —Dermatitis venenata, chronic showing thickening and scaling of skin of whole face. (Dr Grover Wende)



Fig 62.



Fig 63.

Fig. 62.—Dermatitis venenata caused by leather hatband (Dr F Ronchese.)

Fig 63 —Dermatitis venenata of face, caused by hair dye. (Dr H w rd Fox.)

extent. Dermatitis may become universal, a form of exfoliative dermatitis (q.v.) and this may take place suddenly suggesting that degree of sensitivity may increase abruptly

Lesions of contact dermatitis are notably itchy as a rule, more so than their appearance suggests. The hands, forearms, and face are the sites of predilection, although no region is exempt The variations of area and of severity of involvement are not limited.

Such morphologic and out-of-date names as *erythematous eczema vesicular eczema, chronic eczema, fissured eczema* are not sufficient to identify the disease and to satisfy the need for interpretation. Eczema is defined as dermatitis of unknown cause. Dermatitis always has a cause, although this may be difficult to identify Dermatitis due to a dye, para phenylendiamine for example, might at different times in one person manifest a variety of morphologic forms, ranging from bullous inflamma tion to lichenification. Merely to name it erythematous eczema at one time, and lichen chronicus or neurodermatitis at another time would imply failure to comprehend the phenomena manifested

*We include within the meaning of dermatitis venenata* all inflam mations of the skin provoked by contact, whether the agent is a primary irritant which acts with substantially equal effect upon all skins (nitric acid, lye) or is a sensitizer which acts with various intensities on different skins because of hypersensitivity Some chemicals are both primary ir ritants and sensitizers.

If sharp distinction is lacking between chemical traumatic dermatitis and allergic contact dermatitis, excepting number frequency and intensity of contacts, it is equally lacking between contact dermatitis and the hyperergic reaction to the products of parasites reaching the skin from upon it, within it, or via the vascular system from distant foci, dermal or elsewhere. When one judges from the hand alone, one cannot differentiate between pompholyx due to sensitivity to chemicals of known composition, and pompholyx caused by dermatomycosis of the feet Arsenical dermatitis due to intravenous medication looks like contact dermatitis and perhaps is not fundamentally different from it. Dermatitis venenata, however is not dermatomycosis or dermatophytid. We believe that, if one identified all cases of dermatitis venenata, dermatomycosis, dermatophytid, bacterial dermatitis, dermatitis dependent on focal infection (bacterids) dermatitis dependent on food allergy and combinations of these, then few cases of eczema would remain undiagnosed.

Irritation provoked by medicinal chemicals such as mercury is dermatitis venenata of medicinal origin. Allergic dermatitis, such as lipstick dermatitis or nickel dermatitis, is included. We recognize that the etiologic emphasis in the one class is to be placed on chemical trauma, and in the other class on allergic reaction. There seems however to be no hard and fast line of distinction to be drawn between the two. One must interpret the hyperergic response as the physiologic response to some sensitizing irritants, just as purulent inflammation is to be expected as the physiologic response to *Staphylococcus aureus*. Sulzberger and Baer (JInvD 1: 45, 1938) studied dermatitis produced experimentally by related, simple chemicals of known composition (chloronitro benzenes) and showed that the ability of each to produce contact dermatitis in human beings paralleled the ability to produce skin sensitization in guinea pigs and that this property seemed related to the lability of the Cl and $NO_2$ groups. Wise and Sulzberger (AmM 28: 4 16, 1933) studying the reaction to butesin picrate described 3 time periods, those of (1) refractoriness, which may persist for months despite contact; (2) incubation of 9 or 10 days and (3) development of reaction 16 to 48 hours after the contact after allergy has, during the refractory period come into existence Subsequent contacts, after sensitization has been accomplished, take place promptly skipping the refractory period.

The nature of antibodies responsible for contactant allergy has not as yet been determined they must be local, have not been isolated and are not passively transferable (Leider and Baer JInvD 10 4.5, 1948) When sensitivity has developed to one chemical, reactivity to primary irritants of other chemical varieties is not influenced (Haeberlin JInvD 10 27 1948) Eckstad's studies using turpentine derivatives



Fig. 44.—Acneform folliculitis from cutting oil. (Dr. Clyde L. Cummer.)



Fig. 45.—Ragweed dermatitis.



Fig. 46.—Cement dermatitis. (Dr. Sam Sweitzer.)

(abs YBD 1946, p. 560) were interesting the toxic, primary irritant effect was of short latent period, 4 hours or so, and erythema, swelling, even pustulation developed depending on intensity of exposure; the purely eczematous effect in sensitized persons might appear within a few hours or might be delayed even 3 or 4 days, and the most intense exposure flared earliest. If during the sensitizing exposure the skin is necrotic the necrosis appears to protect against the development of eczematous reaction.

Eyelids are tender tissue readily capable of becoming swollen and itchy and are often involved in contact dermatitis. Flexural folds (neck, antecubital popliteal) and the delicate skin of the genital region are commonly attacked. These regions are probably often sites of mediate contact noxae being carried by the fingers. Dermatitis caused by shoe dye, garters, or stockings may provoke eyelid inflammation. Repeated attacks of swelling and itching of the eyelids, with redness, infiltration and loss of flexibility are practically always due to dermatitis venenata. While drops containing atropine may be the cause in a given case of itching lids, one must usually seek noxae through the whole gamut of air-borne water borne medicinally or cosmetically applied occupational seasonal or other contacts with any part of the entire body surface. Fungus allergy may provoke exactly similar response. The eczematous reaction is not different with different allergens.

That dermatitis is due to contact can promptly be inferred from clinical examination for itching ill-defined edges, and absence of pus preclude interpretation as bacterial. Identification of the cause, however is often a complex and tedious business, which involves separation of dermatoses due to parasites from those simply complicated by parasites, or dependent on foci of infection or other internal causes.

Hardening the phenomenon of development by the exposed individual of ability to withstand contacts at one time injurious to him is commonplace, especially in industry. The workman stays on the job despite his dermatitis unless the injury is extreme, and he has perhaps 9 chances out of 10 of becoming hardened as Schwartz (MichSMSJ 39 179 1940) demonstrated. See Peek et al. (IndustM 14 214 1945). The private practitioner is likely to see only the patient who for unknown reasons fail to harden.

**Etiology and Pathology**—Review matter on allergy (p 27). The problems of altered reactivity are gradually becoming clarified. It seems safe to make these generalizations (1) all human beings can develop hyperreactivity to some things under some circumstances (2) the degree of reactivity in a given person varies with the manner of contact and quantities, durations, and time intervals involved (3) clinical manifestations depend on (a) the reactive tissue whether dermal, epidermal, or both, (b) degree of reactivity, (c) location, duration, intensity and frequency of contact and (d) bacterial and medicinal complications that are superimposed. Little is known about why sensitivity appears. Its onset may be sudden after years of previously innocuous contact. The farmer with ragweed dermatitis is an adult who met the allergen for years without having had symptoms. Burns, abrasions, moisture, heat tinea, staphylococcic dermatitis and hyperidrosis render a person more vulnerable. Some people are prone to develop sensitivities and others are not.

Sensitization from the initial substance may spread so as to embrace other substances of related or nonrelated chemical nature and a person who has contact dermatitis is twice as susceptible to other materials as a

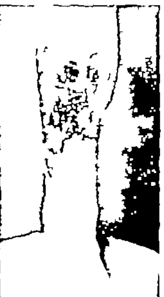


Fig. 67



Fig. 68

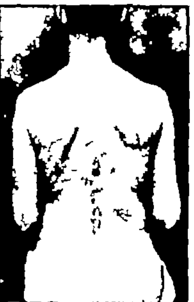


Fig. 69.

Fig. 67.—Dermatitis caused by tincture of iodine. (Dr Howard Fox.)
Fig. 68.—Dermatitis caused by chrysarobin used in psoriasis. (Dr D. E. H. Cleveland.)
Fig. 69.—Dermatitis caused by cement. (Dr Howard Fox.)

person not so affected (Sulzberger and Rostenberg JImm 36 17 1939) Group specificity in epidermal allergy follows a pattern similar to that of serologic reactions, wrote Rothman et al (JInvD 6 191 1945)

While chemical sensitization may succeed dermatomycosis—a matter of significance in industrial dermatology—it is likewise common for nonparasitic contact dermatitis to become complicated with parasitism dermatitis of the neck becomes complicated by seborrheic dermatitis from



Fig 70—Nail lacquer dermatitis. (Dobes and Nippert ADS 49 183, 1944.)



Fig. 71.



Fig. 72.

Fig 71—Dermatitis due t wooden pendants of necklace.

Fig. 72—Dermatitis from handling blueprints, and patch test on thigh positive to potassium bichromate solution (Dr Clyde L. Cummer)

the scalp or ivy dermatitis by dermatomycosis from the feet or dermatitis of the hands by monilial from inconspicuous vulvovaginitis, or perianal and pedal epidermophytosis by medicinal dermatitis in which it is impossible to tell which came first It is such combinations which comprise confusing cases once called eczema.

Agents and their concentrations suitable for patch testing were listed by Rostenberg and Sulzberger (JInvD 2 93 1939) Of some 230 cases seen in private practice drugs caused 71 weeds 31 clothing 21 cosmetics 17 soaps 11 physical agents 5 nickel 4 and matches 2, in the experience of Wilson (NebrSMJ 22 310 1937) Osborne and Hallett (NYSJM 42 1529 1942) listed numerous common irritants.

Patch tests were carefully evaluated by Warren (SMJ 36 425 1943) and untoward results of such tests were studied by Epstein (JInvD 5 65, 1942) Downing (ADS 44 63 1941) and others. New chemicals proposed for use by the public should undergo prophetic patch testing Schwartz and Peck (PHRpts 59 1 1944) suggested. The statistical validity of such testing was evaluated by Henderson et al. (JInvD 6 227 231 1945) Quantitative patch testing technic was designed by Dunn et al (JInvD 6 323 1945)

Epidermitis (swelling vesiculation, necrosis of the epidermis) is a basic change in contact dermatitis (Miller ADS 56 678 1947) Mesodermal inflammation, with capillary dilation, edema, and leucocytic infiltration, also occurs. In some cases the dermis is the shock tissue and the epidermis secondarily becomes acanthotic, hyperkeratotic and variable in thickness. Leucocytic infiltrates in allergic disease contain a relatively high proportion of eosinophiles.

**Excitant Causes of Dermatitis Venenata.**—The list i almost interminable (W bers ADS 35 129 1937) Frequent chemical causes are strong acids and alkalies, turpentine nail lacquer rubber cleansing agents, occupational hazards, incompletely polymerized plastics, medicines, wool t ra, cosmetics fabric finish, mercurial compounds, and formalin. The concentration f the irrita t is an important considera tion (Rostenberg and Sulzberger JIn D 93 1939) Mucosa, as well a skin, may be the site f contact inflammation which does not differ from contact dermatitis. *Cheilitis and stomatiti well as dermatitis of the face or even of the hands, may be* caused by tooth paste mouthwa h, prostheses and other things

Chlorinated Oils, especially dielectric hloronaphthalenes, may induce acne of extreme severity including comedones, milia, and sebaceous cysts, along with the in flammat ry les ons subsequent to them. Hot chlorine compounds and fumes are the act ve agents rather than cold wax (Jones JIndustHyg 23 290 1941) Such acne ha been named according t the product in the man facture f which it wa observed, as perna krankheit halowax acne cable rash (Sulzberger et al.; NYSJM 34 899 1934) All persons exposed to hloronaphthalenes, chlorodiphenyls, or hloro d phenyloxides will develop acne within a few months unless stringent precautions are used (Schwartz and Peck NYSJM 43 1711 1943) The face is exposed and the thigh, groin and umbilical regions are ffected via soiled garments. Coal tar workers are also subject to oil acne but t a less degree than workers with heavy tar distillates and p tch. A person with seborrhea, prone t develop acne should not be hired for such work. Acute yellow trophy as well as mere dermatitis may be caused by chlorinated naphthalenes (Collier Lancet 1 72, 1943) Good and Pensky (ADS 48: 251 1943) described erythematous and vesicula dermatiti too, and oted concomitant complaints f lassitude anorexia, impotence headache alopecia, and loss of weight in their patient Patch test are negat e Chlorophenate moth proofing in f bres may cause oil acne

Oils used lubrication and cutting with ma hine tools provoke *folliculitis* with acneic comedones, pustules and scarring The part affected re especially the hairy forearms and thighs. Prevention can be successful if efficient effort is made to minimize the xposure to oil f the ski thoroughly cleansed after exposure, and if the clothing is kept properly lean no local therapy is necessary ordinarily (Schwartz: PHRpts 56 194 1941 The insoluble cutting oil are the worst offenders (Peck: J 125 190 1944)

Clothing Dermatitis is at first located t the ctual site of usual contact. The noxious agent is usuall resinous fabric fini h (Schwartz et al. J 115 906, 1940) When Nylon hose first became popular it hing of the dorsa of the feet wa first observed to have been caused by them. Faint redness with severe itching soon appeared

on the legs and thighs, later spreading to hands and forearms due to contact during laundering, which women usually do for themselves, and to the eyelids, later becoming universal. An abietic acid ester gum was the irritant in cotton underwear reported by Keil (ADS 47: 242, 1943). Dermatitis from men's shorts, provocative of extreme discomfort and swelling of the genitals, was commonplace in 1942 (Costello and Ryan: ADS 46: 254, 1942, and others). Many synthetic resins are potent sensitizers, to be met not only in garments, but in glue, plastics, etc., and the dermatitis they cause, while extremely pruritic, may persist for weeks after contact has ceased (Schwartz: JInvD 4: 459, 1941). Clothing dermatitis was excellently reviewed by Schwartz and Peck (J 128: 1209, 1945). Dyes, mordants, impregnations, and the textile itself may be irritant as well as the finish. In shoes, the chlorophenol antimildew, glue, dye, polish, chrome or formol tanning agent, or other component may be the specific irritant (Shaw: ADS 49: 191, 1944).



Fig. 73.—Dermatitis of eyelids from matches. (Dr. D. E. H. Cleveland.)



Fig. 74.



Fig. 75.

Fig. 74.—Matchbox dermatitis. (Dr. D. E. H. Cleveland.)
Fig. 75.—Matchbox dermatitis. Close-up of Fig. 74.

When a garment is suspected of being the cause, the patient is instructed to wear nothing but clothing which was already 6 months old at the time his dermatitis began. Such clothing, previously worn and found harmless, may be trusted unless subsequently it was exposed to chemical contamination. It is probable that an injurious agent would be removed if the garment were subjected to repeated cleansing with carbon tetrachloride

followed by soap and water and thorough rinsing. Boiling alone will not remove it. Soap, starch, bleach, bluing, laundry antiseptics, or substances from cleaning fluid may remain in a fabric rendering it irritant even though it may not have been irritating at the time of purchase. Garment dermatitis is a serious matter of significance to the public health. One wishes hypoallergenic garments could be purchased.

COSMETIC DERMATITIS.—Cosmetics including perfumes, hair dyes, scalp cleansers and tonics, depilatories, deodorants, face powders, creams, bleaches, lotions, rouge, lipstick and nail preparations may contain many potentially provocative chemical constituents (Tulipan: ADS 38: 906 1938).



Fig. 76



Fig. 77



Fig. 78

Fig. 76.—Iodoform dermatitis. (Dr. J. W. Perkins.)
Fig. 77.—Wrist watch strap (leather) dermatitis. (Dr. F. Ronchese.)
*Fig. 78.—Ulcers due to droplets of chromic acid solution used in chrome plating.*



Fig. 79.—Onychia caused by sugar in a bakery employee. (Dr. Clyde L. Cummer.)

Composition and hazards of numerous cosmetics were briefly elucidated by Walcott (ADS 41: 81, 1940). There is much information in Harry's Modern Cosmeticology (Chemical Publishing Co., 1940). A typical dermatitis paralleling the blepharal margins is produced by the antioxidant of the rubber of eyelash curlers (Curtis: ADS 8[illegible]: 702, 1945). Lipstick dye may cause systemic allergic phenomena as well as cheilitis (Hecht: J 113: 410, 1939; Zakon et al.: ADS 56: 499, 1947). Dentifrices provoke cheilitis and dermatitis of the cheek and chin, and even dermatitis of the hands at times (Heinkamer: ADS 41: 802, 1940). The yellow dye of a leg make-up was the faulty ingredient identified by Ellis (ADS 49: 107, 1944). Hair lacquer caused much trouble at one time, the irritant being synthetic resins (Schwartz: PHRpt 58: 1623, 1943); and the mother's hair lacquer irritated her infant in [illegible] cases recorded by Plotz (AmJDisChild 69: 400, 1944). Hair dye poisoning, even a fatality, was discussed in an interesting editorial (BMJ [illegible]: 490, 1943). In nail lacquer the formol-sulfonamide resin was to blame in cases of Simon (BMJ 31: 187, 1943), while nitrocellulose and solvents, as well as synthetic resin, were noxious in cases of Dobes and Nippert (ADS 49: 183, 1944; see also Madden: [illegible] 49: 19[illegible], 1944; Osborne et al.: [illegible] 44: 604, 1941; Silver and Chiego: JInvD [illegible]: 361, 1939). Nail lacquer dermatitis rarely affects the hand, but provokes circumscribed lesions readily confused with parasitic rather than chemical dermatitis of the areas to which fingers go, such as eyelids, ears, trunk, and vulva. A pruritic patient with any dermatosis, such as scabies, is well advised to omit nail lacquer until her skin is clear, for where she itches she will scratch, and she may develop nail lacquer dermatitis as a complication.

INDUSTRIAL DERMATITIS.—Since dermatitis venenata is of such significance in industrial medicine its control assumes important proportions; and its prevention and treatment have been the subject of numerous contributions (Schwartz, Tulipan and Peck: *Occupational Diseases of the Skin*, Lea & Febiger, 1947). The principles of interpretation are those of contact dermatitis. The principles of treatment are in general the prevention of contact by suitable protection, such as gloves, chemical detoxification of harmful substances before they have produced damage, identification of noxae as well as susceptible employees by means of patch tests, and similar testing of materials before they have been admitted to public use.

A part of a monographic symposium concerned with the problems of industrial dermatology, Sulzberger and Finnerud (J 111: 1[illegible], 1938) contributed a clarifying tabulation, which should be studied carefully. See also Lane et al. (J 118: 613, 194[illegible]). Instructive examples of the working out of specific problems were presented by Schwartz (MOO [illegible]: 34, 1939). Stigmata of occupation, such as scars and calluses, were interestingly collated by Ronchese (J 123: 92[illegible], 1943).

INDUSTRIES COMMONLY AFFECTED.—Workers in certain trades are prone to skin eruptions, and many cases are seen in connection with the Workmen's Compensation Act. Analyzing more than 500 occupational cases, Klauder (ADS 48: 579, 1943) found the causes fell in the category of trauma in one fourth, primary irritant in one-fourth, cleansing agents in one sixth, sensitizers in one eighth, and petroleum products and water maceration in about one tenth each. In our Middle West experience cleansing agents are to blame in perhaps half our cases.

Rubber dermatitis is commonly due to sulfur monochloride used in the curing process. It can be rendered non-irritant by treatment with an alkali such as 4 per cent sodium hydroxide solution. An accelerator such as paranitrosodimethylaniline may be the irritant (QMN: J 113: 1[illegible], 1939). Mercaptobenzothiazol caused most of the trouble studied by Downing and Marcussen ([illegible] [illegible]: 163, 1944). Rubber and rubber cement are used in shoes and may cause dermatitis of the feet (Anderson: CalWM 61: 63, 1944). An antioxidant in rubber gloves caused depigmentation, but repigmentation eventually occurred when contact had been interrupted (Oliver et al.: ADS 4[illegible]: 993, 1940).

Cement workers are harmed by alkali. Lime particles are slaked on the skin in perspiration, and the skin becomes dry, hard, thick, and liable to painful fissuring. Ulcers of the nasal mucosa, as well as of the skin, may result. Secondary infection with pyogenic or fungus organisms is likely. Prevention lies in control of dust and cleanliness of the workers. Goggles protect the eyes, lanolin helps keep the skin dry, and boric ointment protects the nostrils (Meherin and Schomaker: J 11[illegible]: 13[illegible], 1939).

MEDICINALS are common causes of contact dermatitis. Examples include mercurial ointment (Bello: AmJMSc 201: 736, 1941), iodine (Jacobs and Colmes: JLabClinM [illegible]: 802, 1940), opiates (Jordan and Osborne: J 113: 1953, 1939), procaine (Goodman: JInD [illegible]: 33, 1938), ephedrine (Fulton et al.: JAllergy 3: 493, 1932), antiseptic baby oils (Lapen: AmJDisChild 63: [illegible], 194[illegible]), ammoniated mercury (Samitz: ADS 50: 10, 1944), penicillin (Barker: Lancet 1: 1[illegible], 1945), and sulfonamides with a litera-

| Employment | Irritant |
|---|---|
| Agriculturists | poison ivy ragweed other plants ticks, chiggers sporotrichosis fertilizers, sprays insecticides fungicides; sunlight causing cancer milk can cleansers, irritant soaps; chlorine i privies |
| Aircraft workers | zinc chromate primer red s, glues, oils, acid fumes |
| Automobile workers | cutting oils, solvents, brake fluid, paint, lacquer |
| Bakers | flour or sugar; cotton seed oil and potash the former being used in bread, the latter, in pretzels; whitening agent essential oils of flavoring |
| Barbers | quinine mercury capsicum, arsenic sulfur cantharides |
| Briquette makers | coal tar pitch causing photosensitivity melanosis tar acne keratoses, epithelioma |
| Butchering | anthrax, foot and mouth disease erysipeloid, hog itch, ac to pemphigus, onycholysis from pancreatic juice verruca necrogenica |
| Candymakers | sugar chocolate cinnamon oil of cassia citrus oils, vanilla other flavoring agent |
| Canning | fruit vegetables citrus oils peach juice and fuzz, pineapple juice figs, tomatoes potatoes, carrots, and lettuce |
| Carpenters | various wood sawdust plywood adhesives |
| Chemist | many irritants handled by them |
| Compositors | benzine bichromate |
| Cook | cleansers, soaps insecticides, flour bleach (benzoyl peroxide) |
| Cosmeticians | cold wave thioglycollates, hair dye (paraphenylene diamine) cuticle softeners, nail lacquers, hair bleaches and shampoos |
| Dentists | novocain soap, prosthetic plastics |
| Electrician | chlorinated hydrocarbon dielectrics |
| Electroplaters | cyanide various acids, chromates |
| Electrotypers | copper sulfate hydrochloric acid |
| Explosive makers | T.N.T. tetryl, picric acid and picrates, mercury fulminate ammonium nitrate |
| Exterminators | arsenic formalin, sodium fluoride lead, pyrethrum |
| Fishermen | bites, abrasions, stings, infection |
| Foresters | poisonous shrubs, sprays containing arsenic and lead |
| Furriers | arsenic dyes ffs, insecticides |
| Gluemakers | alkali gelatin phenol formaldehyde urea formaldehyde styrene alkyd allyl resins |
| Grocers | handling of sugar and flour cleansers roach powder |
| Interior decorators | dyes and fabric finishes |
| Laundry workers | alkaline soaps synthetic detergents, antiseptic after rinses (phenyl mercuric acetate) bleaches |
| Machine tool operators | cutting oils cleansers antiseptics in oil |
| Milliners | dyes, arsenic |
| Nurses | bichloride formalin, medicated alcohol, lye cresol or other antiseptics, morphine penicillin, streptomycin |
| Painters | *turpentine varnish remover arsenic, linseed oil, dyes* |
| Petroleum workers | oil, gasoline cleansers |
| Photoengraving | acids, aniline chromium, alkalis, formol, glue |
| Photographers | pyrogallol, metol, caustic soda chromates, dyes, lacquers |
| Plate printers | inks, solvents dyes, cleansers |
| Polishers of metal | oxalic acid turpentine bichromate |
| Printers | arsenic artificial coloring, hydrocarbon in inks, chromate in photostats, cleansers |
| Seamstresses | textile finishes, dyes wool, thread, yarn |
| Shoemakers | chrome tanned leather dyes, cements, polishes, solvents |
| Stenographers | cleansers, cosmetics (rarely carbon paper) |
| Surgeons | antiseptics used in scrubbing up rubber gloves, novocain |
| Tanners | bichromat hydrochloric acid |
| Welders | actinic burns, chromium fumes, zinc chloride ammonium chloride fluoride fluxes |

ture too extensive to require quotation. Proprietaries and their compositions were listed by Underwood et al. (J 130: 258, 1946) along with warning against the mixed ventures of self-medication and age ast the urge to stick something on it.

Of 9 patients intolerant of Aquaphor 8 were sensitive to cholesterol (Ellis: ADS 56: 801, 1947). Streptomycin was the cause of eczematous dermatitis in 4 nurses shown to be hypersensitive by Crofton and Foreman (BMJ 2: 71, 1948).

METALS of many kinds may cause contact or occupational dermatitis. Aluminum does not, but dermatitis attributed to it is generally due to oils or cleansers. Nickel dermatitis is common, and the substance may touch the skin in the form of spectacle frames, zippers, pins, garter fasteners, jewelry and the like (Downing: ADS 41: 58, 1940). Chromium, chromate, and dichromate are met by the population at large as well as by workers in industry and these are potent causes of eczematous dermatitis as well as painless sloughing ulcers of fingers and nasal septum (Vaccaro IndustM 10 246, 1941). Workers exposed to vapors of antimony developed it by varicelliform eruptions (Fell abs YBD 1940, p. 60). Lithium burns are alkali burns like those from sodium (QMN J 126: 268, 1944). Beryllium produced severe papulovesicular and ulcerative dermatitides (Van Ordstrand et al. J 129: 1084, 1945). Selenium provoked purpuric contact dermatitis (Pringle BJD 54 54, 1942). Beryllium caused conjunctivitis, papulovesicular rashes, and ulcers requiring curettage (Edit. BMJ 2 231 1946).

PLANT AND WEED DERMATITIS.—Plants are among the commonest causes of contact dermatitis (Shelmire: SMJ 33: 337, 1940). Poison ivy the primrose, and ragweed are noteworthy offenders.

*Poison ivy dermatitis* results from contact with the oleoresin, which may be conveyed indirectly as well as immediately but vesicle fluid and smoke from the burning plant are not noxious. The antigen, which attaches itself firmly to the epidermis, is probably eliminated by exfoliation. Hydrourushiol, a stable crystalline substance to which all are sensitive who are sensitive to poison ivy, was synthesized by Mason (JAmChemSoc 67: 1538 1945) and quantitatively standardized patch tests were designed by Dunn et al. (JInvD 6 323 1945). Not all human beings exposed to strong extract of poison ivy develop sensitivity (Simon and Loiterpelch JInvD 2 143, 1939) and it is said that individuals with atopic dermatitis cannot be sensitized. If the skin is painted with the extract and then after 12 hours is extirpated, generalized sensitivity nevertheless develops. To prevent systemic absorption and reaction, circumvallation of the painted island must be prompt and must go through to muscle so as to interrupt lymphatic absorption (Landsteiner and Chase JExpM 69:767 1939). Poison ivy oak, and other variants represent single polymorphic species with habitat variations (Shelmire JInvD 4: 337, 1941).

Many individuals are sensitive both to poison ivy and cashew nut shell liquid (Keil et al. Sc 102: 279 1945). The resins of cashew are phenol formaldehyde substances used in mucilage and varnish (Schwartz et al. IndustM 14 500 1945).

*Ragweed dermatitis* occurs in adults and rarely in children. Its features are characteristic the seasonal incidence annually repeated, during July and August and maximally in September disappearing with the first frost; the redness, swelling, and itching of the eyelids and inflammation of the exposed surfaces, especially the hands, wrists, ankles and face the exacerbations which occur after hunting, weeding or otherwise contacting the plant; and the local reaction with distant flare on patch-testing. The dust of ragweed in grain and flour may serve as an industrial hazard (Jordan et al. ADS 46: 721 1942). Hyposensitization by oral administration of the specific oleoresin is practicable (see J 123: 733 1943).

*Dhobie mark dermatitis* is the contact dermatitis provoked by the laundry marking material derived from the ral or bella gutti in India (Livingood et al. J 123 23 1943). This potent sensitizing substance is not destroyed by boiling. The disease was long confused with dermatomycosis.

*Plant dermatitis* was reviewed by Shelmire (J 113 1085, 1939). During the first few years the dermatitis is seasonal, corresponding closely to the growing season of plants. At the onset the eruption is usually erythematous, scaling and pruritic. Exacerbations caused by massive exposures are characterized by increase in erythema, swelling and oozing and occasionally by fine vesiculation. With seasonal recurrence dermatitis becomes more widespread, owing to increase in sensitivity and manual spread of antigenic oleoresins to areas of the body covered by clothing. Thickening of affected areas follows trauma occasioned by protracted scratching and rubbing. Seasonal attacks extend further into the winter before completely healing. Sooner or later the eruption becomes perennial—extremely severe during the growing season of plants with remissions during the winter months. Erythema, edema, oozing and crusting disappear but pruritic lichenified areas often persist until the new spring weeds return. The

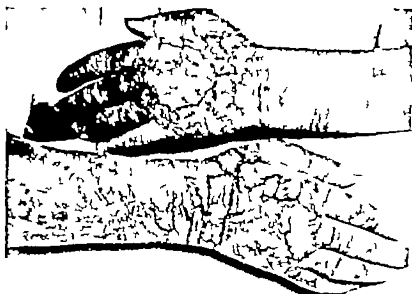


Fig 30 —Dermatitis i a grocer cause undetermined.



Fig 31 —Poison i y d rmatitis, cut (Dr H ward Fox.)



Fig. 32.—Toilet w t photosensitization led t this curious pigmentary lesion. (Simons YYD 1939 p. 135 )

sites affected are usually the exposed areas such as the face, neck, backs of the hands, wrists and ankles. The eruption gradually spreads to involve the forearms and legs. In men the penis and the anterior surface of the scrotum are often erythematous and thickened. Occasionally patchy areas of dermatitis appear over the trunk and groins. In the more widespread and long-standing cases those areas which are more easily irritated by external agents, such as the face, the sides and front of the neck and the flexures, become markedly lichenified. Prolonged healing time is characteristic. If patients with weed eczema are hospitalized and contact with vegetation is absolutely avoided, disappearance of the eruption usually occurs within from 2 to 6 weeks. If these patients are ambulatory but avoid actual contact with weeds, the healing time is frequently prolonged for from 6 weeks to several months since they continue to come in contact with small amounts of the antigenic oleoresins through contaminated work clothes, tools, pets, udders of cows. Most of the affected persons are farmers and others whose occupations bring them into almost daily contact with vegetation. Each weed contains an ether-soluble oleoresinous dermatitis-producing fraction and a water-soluble albuminous hay fever-producing fraction. This can be demonstrated by tests on a person in whom dermatitis develops from contact with a specific weed and hay fever or asthma from inhaling its pollen. Patch tests on this person with portions of the antigenic plant will evoke a delayed eczematous reaction. If all the dermatitis-producing oleoresin is removed by repeated ether extraction, the remaining de-oiled residue which still contains the atopic fraction, will then evoke the typical immediate urticarial scratch or intradermal hay fever reaction. Eczema-producing oleoresins appear on the leaves, stems, and flowers of many weeds as tiny globules of oil readily seen with a hand lens. These oleoresins are sticky and adhere tenaciously to the skin or clothing. Contact of sensitized persons directly with the plant or with contaminated intermediary objects is followed by dermatitis. Previous contact is necessary for the development of sensitization to a plant. When weed-sensitive persons were tested on unbroken areas of the skin by the uncovered method, many developed an apparent flare-up of the eruption. Focal flare-ups did not occur when the same persons were retested and the patch sites were completely covered to prevent manual transference of the oleoresin. All attempts to demonstrate antibodies in blood serums of weed-sensitive persons by the Prausnitz-Kustner method of passive transfer have failed.

WAR MATERIALS.—Mustard gas, $(CH_2ClCH_2)_2S$, is a vesicant; the effects are delayed 2 or 3 hours in onset; then there appear nausea and vomiting, burning of the eyes, pain in the throat, and hoarse cough, intense conjunctivitis temporarily blinding the victim, redness of the skin followed by blistering and brownish staining of the exposed skin and the flexures, inflammation and necrosis of the pulmonic mucosa leading to septic bronchitis and to bronchopneumonia. Death results ordinarily only as a result of septic complications and later than the first day. Intense exposure may produce gangrene. See Cole et al. (ADS 39: 45, 1939); Goldman and Cohen (J 114: 2200, 1940); Sulzberger et al. (JIn D 8: 365, 1947).

Lewisite, an arsenical mustardlike poison of great potency, produces erythema and bulla formation along with arsenical intoxication. British Anti-Lewisite (BAL) or 2,3-dimercaptopropanol, which given intramuscularly in an oil solution is an effective antidote (see p. 4[?]).

Tear gas (CN) may cause vesicular dermatitis, and is a sensitizer (Ingram, BJD 54: 319, 1942).

Tetryl (trinitrophenylmethylnitramine), an explosive in the manufacture of which workers routinely develop dermatitis with itching, burning, erythema, edema, epistaxis, sneezing and coughing, and a typical yellow staining of the skin and redness of the hair. Most workers undergo hardening and may persist with their work (Eckhardt, J 125: 136, 1944). Fulminat causes discrete erythema of hands, forearms, and face, and TNT produces a typical pompholyx-like eruption (Swanson, BJD 56: 44, 1944).

Radiation injuries of all degrees of severity and of local or general extent may occur in connection with atomic fission work (see x-ray injuries).

CONTACT PHOTOSENSITIZATION (BERLOCQUE DERMATITIS).—Pigmentation results from the application to the skin of toilet water containing oil of bergamot or some other essential oils followed by sunlight or quartz light. The lesions appear as dark red areas changing to brown, slightly mottled with red. Certain grasses may by their oils so sensitize the skin that dermatitis and pigmentation of striking linear and crisscross configuration follow contact with them (Sandler, J 11[?]: 411, 1939). The furocoumarines of plant juices are responsible for the abnormal responsiveness to light of 3100 to 3700 Å such that exposed skin may even blister while covered skin does not react. Parsnip (Jensen and Hansen, ADS 40: 566, 1939), lime oil (Sams, ADS 44: 571, 1941) and agrimony (O'Donovan, BJD 54: 30, 1942) have been care-

MEN WOMEN BOTH SEXES

Fig. 31.—Men Cosmetics include sha ing cream, l tion, powder perfume, soap, dentifrice, mouthwash. Articles ( trousers pockets include leather nickel, matches, matchbox, lighter lighter fluid, tobacco, keys, wallet. Women Cosmetic include those of ( ) hair w set, lacquer dye, bleach, permanent wa e, shampoo, pomade, cologne, medication; (b) face powder perfume, creams, rouge, powder puff, soap, lentifrice, lipstick, mouthwash ( ) eyes; mascara, lash dye, rubber of lash curler eye drops, any agent affecting head, f ce, or hands. Garment include wool, cotton, silk, rayon, nylon, fur dyes, rubber il lage, bedclothing, day and night clothing, f bric finish, fasteners. Sanit ry chemicals include deodorant, douche, jelly, pessary suppository, condom, napkin, powde bath salts, w ter softener perfume. H ve irritant includ silk, rayon, nylon, dye, fabric finish. Both sex spectacl frames (Nl, Cr plastic, cleaning fluid for lenses) oral nd f cial irrita ts such gums, dentifrice mouthwash, denture adhesive, foods (dyes, essential oils) drugs toilet seat arnish, disinfectant jewelry lacquer metal straps. Clea ning agents nd medicines re common irritants. D-dye F f bric finish; L-leather; N-nickel; R rubber (Dr George L. Waldbott.)

fully studied but photocatalysis remains ill understood. Tar and pitch handlers may develop melanosis as an occupational photosensitization phenomenon (Foerster and Schwartz: ADS 39: 935, 1939)

**Diagnosis of Dermatitis Venenata.**—In acute cases (initial reactions) the abrupt onset history of exposures, location itchiness, erythematous and vesicular character of the eruption and ill-defined margins serve to make the diagnosis of contact dermatitis easy But to unearth the particular cause is less simple. The longer the dermatitis has endured the more difficult it is, as a rule, to discover the allergen Flares give clues contact must have been made a few hours before the flare Location of onset is the first clue to the nature of the noxious agent. The manner of reaching the skin obviously influences the location. Allergens reaching the skin as air-borne dust settle in greatest concentration on exposed parts, moist parts, and where clothing constricts. In dermatitis caused by shoes (Niles J 110 363 1938) vesicular eruptions appeared on the feet when the offending shoes were worn, and disappeared when they were not. Dermatomycosis was ruled out by the relationship of flare to the wearing of the shoes, by positive patch tests, by absence of demonstrable fungi, by severity of the itching which seemed disproportionate to the visible dermatitis, by freedom of interspaces from involvement, by predilection for the dorsum of the foot and by sharp margins of irritated areas. Not all vesicular eruptions on the feet are tinea Contact dermatitis is never primarily pustular secondary infection from the skin flora, contaminants, or focal sources render it pustular when it is. The patient s understanding and cooperation are of primary importance in the search in the usual case it is imperative for the physician to give the considerable time necessary for the patient s enlightenment (Sulzberger and Rostenberg JAllergy 6 448, 1935)

Diagnosis is proved by cure of the disease when the agent is completely avoided, and recurrence of the disease when the specific agent again touches the skin.

**Prognosis.**—Removal of the cause is followed, usually within a few days or weeks, by recovery Repeated attacks are expected, until the cause is identified and contact is avoided. A known and carefully avoided agent may be met accidentally or inadvertently Efforts to desensitize are in general less successful than avoidance. Sensitization may disappear if contact is avoided for many months, or the degree of sensitivity may diminish greatly

| Complication | Possible Explanation |
|---|---|
| Pruritus with excoriation | Medical dermatitis, *as from ammoniated mercury* |
| Lichenoid areas | Seborrheic dermatitis, chronicity and perhaps medicinal dermatitis |
| Papular vesicular and pustular lesions with folliculitis | Staphylococcic parasitism, abetted by the mechanical effect of salves exogenous, or from oral, prostatic or other focus of infection |
| Vesicular oozing and crusting | Streptococcic parasitism, exogenous, or from oral, genital or other focus of infection |
| Chronic vesicular and scaly dermatitis | Mycotic complication from toes, vagina, or other sources, and medicaments |

**Treatment.**—The basic principle is to remove the cause One must give the patient symptomatic relief while the skin heals. Effort is directed



Fig 84.—Pathology of dermatitis venenata. *Top* Edematous degeneration of superficial epidermis (? poison ivy). *Middle* Slight epidermal edema and mild inflammation, patch test with an external antiseptic. *Bottom* Vesiculation and inflammation, patch test with turpentine (Miller, ADS 56 678, 1947)



Fig 43.—Pathology of dermatitis venenata *Top* 1 tense vesicular epidermal reaction to hair dye *Middle* Vesiculation eczematous dermatitis. *Bottom* Intense vesiculation, poison i y (M D Arch 56 678, 1947 )

at *keeping something off the skin not at putting something on it* No medicine can force an injured tissue to heal There need be no haste to identify the cause. Remove all possible causes, relieve the patient, then seek the cause.

If contact has occurred within a few hours, but reaction has not as yet set in then the removal of the irritant from the skin may be possible Soap and water or alcohol at this time may be urgently needed and successful whereas, a few hours later this same treatment would do harm In ivy poisoning allergen may be present even after reaction has set in.

Chemical neutralization of many dermal irritants can be accomplished. Sodium thiosulfate is the antidote for iodine and chromates, sodium bicarbonate for formol and potassium sulfite soap for TNT for example (Anderson ADS 49 176 1944)

Prevention of contact may be obtained by discarding objects such as shoes or furs. Often it is difficult to convince a patient that one solitary momentary contact is sufficient to undo the benefits of two weeks of isolation Sometimes mechanical means (gloves, petrolatum boots) or chemical means (baths, soaks, detoxifying agents) may be used to interrupt the contact or the sufferer may learn what not to touch or where not to spread the contact or a workman may be shifted to a different job so that his contacts are different Protective ointments are a last choice, not a first one in industrial dermatitis, though they encourage the worker to wash. Better measures are a clean, tidy shop with equipment designed and processes planned to prevent contact with hazardous chemicals, and ample facilities for use of clean clothing and selected cleansing agents so as to minimize the workman s contacts (Schwartz)

Such solutions are easy comparatively if the allergen is known But some allergens are so widely disseminated or of such ubiquitous occurrence that avoidance may be difficult Nitrocellulose wax and sulfonamides are such agents One may apply talc to keep the skin dry rather than grease, which would simply cause particulate irritants to adhere the more. It may be impossible to move the individual from his occupation or to protect him or to desensitize him as in some cases of ragweed dermatitis. Under such circumstances we admit defeat

When the allergen is not known the avoidance of every possible agent is desirable Unless the patient is considerably distressed by his disease, he will not ordinarily be willing to be hospitalized, but hospitalization, with complete control of the environment separating the patient from his home clothing hair tonic toothpaste garden, potted plants, sofa cushions and insect powder is an effective way to bring irritation under control.

**When the Injurious Agent Is Unknown,** but the diagnosis f chemical injury by contact ha been made the technic of cure may be put in algebraic form (Sutton JMoSMA 41 481 194 ) Let chemical items a, b, be all the chemical that touch the skin then

$$a + b + \quad + \quad = \text{disease}$$

Let no item touch the skin unless it is known to be harmless. Then

$$a + b + \quad a \quad b \quad = 0$$

If all contacts except trusted nes are n fact removed disease will disappear within one or tw weeks, rarely longer If disease does ot steadily f d but does flare after the effort has begun the implication must be accepted that while the theory i right the practice has failed and effort must be redoubled to make cert that an unidentified injurious agent will be l minated.

After elimination has succeeded as attested by the fact of uninterrupted improvement, then of a, b, c at least one item is injurious. The status of the patient at this moment, perhaps one or two weeks after the initial instruction in the avoidance of everything, is the relieved but discommodated state of freedom from disease and isolation from all contacts. The task is half finished, and the patient's skin is now ready to serve as the testing ground for the items previously eliminated. If contact with all were replaced at once no information would be gained from the subsequent flare. But if a is replaced, and 24 hours later b is applied, and later c, according to a written tabulation of items to be tested by schedule, then identification of the poisonous item is straightforward. For on contact with that item, the disease flares, usually first evidenced by itching which starts within 4 to 8 hours. If a, b, c are so replaced in their usual form of contact at 24 hour intervals, then identification of a and b and c intact sheep and wolves is a matter requiring rarely more than one week of purposeful effort. It is common to relieve the patient in one week and to identify the cause in another two weeks of endeavor accomplishing complete cure in a month or less.

Hypothetical Case Presentation.—June 1 1949. Mrs. X, 30-year-old white woman, requests medical service because of itchy eyelids. The skin of the lids is wrinkled leathery flaky excoriated but not exudative. Disease has existed with no great change in intensity and no conspicuous flares for 3 years. There is no other disease or area of dermatitis. The interview:

Madam, your skin disease is caused by some chemical which touches your eyelids. Germs are not concerned and your interior food or function, is not pertinent. No medicine exists which will make your eyelids heal. You will be cured and you can only be cured, by avoiding that which on touching your skin poisons it. You and I, as we sit here at this moment do not know what poisons you.

Then, doctor how can I escape the poison?

If nothing touches your face except chemicals which are certainly harmless, then surely your disease must fade and disappear. In order to eliminate all contacts except the certainly harmless ones, you will be put to the trouble of eliminating many chemicals you didn't need to—we shall eventually know which chemicals are which—but for the next week, I want nothing to touch your face except (1) air (you can't avoid it but you don't need to contaminate it by scattering soap powders indiscriminately) (2) water (it is harmless—things in water are often harmful, but water is not); (3) petrolatum (I have seen only 2 people in 15 years of dermatologic practice whose skins would not tolerate petrolatum); (4) old cotton or linen garments, towels, sheets, and pillowslips (do not allow residual soap, starch, bluing or bleach to remain in these please; but the cellulose of which they are composed is trustworthy), (5) hands (which must be free from lotions, creams, nail lacquer etc.) and finally (6) the utensils and foods you use in eating (silver is harmless, and you've got to eat)

My face may be touched by nothing but air water petrolatum, cotton or linen, and uncontaminated hand? I may eat and drink what I wish? All right, doctor but how do I wash, or clean my teeth or relieve my itching if I may not apply a medicine?

I have listed the things you may touch, a short positive list. I have not tried to list the multitudinous things you may not touch, for the negative list is not short and is not determinate. If I don't say touch it, don't. Wash with water and dry with a towel. You won't be as clean as you like but you'll be as clean as you need to be. Cleanse your teeth with table salt or baking soda—I can trust them—after all, you'll only have to live this way for a week or so. As for relief of itching, use just enough petrolatum to keep the skin from feeling as if it would crack, and lay on your itchy lid a towel wrung out in cold water. Petrolatum would not be suitable if your trouble were poison ivy; it would spread the irritant around. Apply the cold compresses for as long as you desire any time you desire. They will relieve you as well as any medication we could choose and cannot harm you. Among the many things you may not touch are soaps of any kind powder rouge creams, perfumes, shampoo, medicines hand lotion, and nail lacquer. Don't put any medicine in your ears, eyes, nose or mouth or on your skin. Since we do not in your case, suspect lipstick, you may use this so that you will not feel too undressed—a patient's morale must be considered—and you may use cornstarch for face powder if you wish.

What makes me get well doctor if I do nothing but avoid a poison?

An injured skin is analogous to an injured bone. In treating a broken bone, the physician basically puts its ends together and leaves it alone. It heals itself. Your skin will heal when nothing interferes with its healing. In the case of the fracture, the patient requires morphine perhaps or aspirin, but medicines do not cure him. They

enable him to live more or less comfortably through the period of time that healing requires. The cold compresses and petrolatum will do for you what the sedatives do for the patient with the broken bone."

"Well, I'll give your plan a try."

"If you comprehend the purpose you will probably cooperate faithfully. Please let me see you a week from today."

June 8, 1948. Mrs. X returned stating that her eyelids did not change much for the first 3 days, then improved steadily. There was no flare; itching became less, and the cold compresses and petrolatum proved quite comforting. Improvement is plainly visible.

"We may judge," the doctor says, "that you have successfully avoided the poison, although this has inconvenienced you to some extent. We must now arrange for you to live normally instead of living in chemical isolation. Of the many things you have been denied, what would you like to put on your face first?"

"Soap, then rouge, powder and cold cream. If I could use these and have my hair shampooed I'd be satisfied."

"We must plan these contacts so that if any of them flares your disease we will recognize it. Write down a list of items to test and test one each day, designating of course the particular brand of toilet article you propose to try. Apply one item each day in the manner in which you ordinarily apply it. Let me see you when your disease flares. Do you understand your instruction?"

"Perfectly, doctor. This seems almost too easy. Other physicians gave me x-ray treatments, intravenous and other shots, a cabinet full of expensive prescriptions, the alphabet of vitamins and quite a series of food allergy tests. Why, for two years, before I met you, I ate no eggplant or kohlrabi whatever and nevertheless itched furiously."

"The therapeutic technic of other physicians is not a subject for my comment but one may say that not all human beings are guided exclusively by crystalline intellectual function. I myself have prescribed a blood purifier. I was weary at the time, and the patient asked for it. Follow your instructions and let me hear from you."

June 13, 1948. Mrs. X returns, her lids swollen, red and itchy. She says, "Doctor, I used soap during the afternoon of our last interview, rouge the next day and powder the next without trouble. But last night I applied cold cream as I retired. This morning my lids were again swollen and itchy."

"You and I now know that this brand of cold cream poisons you," the physician explains. "You will get over this flare in a few days. Use the cold water compresses as you did before. Since we now know a cause—perhaps the cause—it would now be appropriate to give you a little x-ray therapy to hasten your relief. When you have cleared up, try Blank's brand of cold cream. The Journal accepts this firm's advertising which claims that few people are allergic to its products. Seldom indeed do I find a person being poisoned by more than one chemical, although it is not rare for an individual to meet his poison in several different guises. Take for example Mrs. Z, whose poison was nitrocellulose. A few years ago her spectacle frames, the handles of her brush and comb, and her patent leather slippers and handbag each poisoned her. When she and I finally worked that problem out she later flared after handling ping pong balls. As for you, however, I surmise that your troubles are over."

"Doctor, [illegible] appreciation knows no bounds."

"We accomplished your cure by prescribing nothing for you, madam, with meticulous care."

Sodium thiosulfate intravenously, 0.5 gm. the first day and 1.0 gm. the second, third, fifth and seventh days, was said by Ormsby (Mich [illegible] 37:135, 1938) to aid in overcoming hypersensitivity. We doubt its efficacy.

Allergic dermatitis may persist for days or even weeks after the cause has been removed. It is during such a refractory period that a physician impatient for benefit in a case of distressing dermatitis of unknown external cause changes from one medicine to another in the futile expectation of finding something that will bring about healing. As in the case of a wound, healing depends on action of tissues, not on salve that is applied. In shifting from one application to another great risk is run of applying a medicine to which the patient is sensitive. One does best by prescribing the simplest and blandest of agents, adhering to their use if

one is certain they do no harm. One may undertake patch testing with individual ingredients of proposed salves to make certain that they do not irritate. Exfoliative dermatitis has resulted from the application of ammoniated mercury ointment to some minor inflammation, with the development of spreading mercurial dermatitis not recognized as such and treated with more mercury.

X ray therapy desensitizes locally. This is probably brought about by immolation of fixed cellular elements responsible for sessile antibodies. Reactivity generally returns within from 3 to 6 weeks after this nonspecific desensitization. If the same local hypersensitizational dermatitis is treated time after time with x rays, the eventual result is an x-ray burn. The proper use of roentgen treatment in contact dermatitis, and in dermatitis of any origin, depends on the rational implications of this fact.

Benadryl and other antihistamines are helpful when an urticarial element is prominent in the reaction of the patient to the poison, but in fairly pure epidermitis these do not allay (Blumenthal and Rostenberg, MAnnDC 16 86, 1947).

We have found the simplest of medicines satisfactory. In acute dermatitis of contact origin the skin may be freed of previously applied greases by means of benzine. White petroleum jelly is put on to protect denuded nerve endings, and soft clean towels, wet with plain cool water, are superimposed. This is comforting and it is bland. The patient is denied coffee, and may be given aspirin 5 grains every three hours unless intolerance occurs. What the tired, itching patient wants is respite from bedevilment by his skin; then he will sleep.

If no allergen remains and no secondary infection exists, petroleum jelly and water are wholly adequate. Compresses should be moist, not dripping, and cool, and should act like a blotter in absorbing exudate rather than rendering the skin soggy and macerated. They should be left in place not longer than half an hour, but may be repeated as frequently as the patient desires. If they are medicated they should not be allowed to dry on the skin, for as the water evaporates the concentration of solute increases until it may irritate. Aluminum acetate, half a level teaspoonful to a quart of water, made up in a milk bottle and poured from that onto the towel, is convenient and satisfactory.

If secondary infection occurs, 1 or 2 per cent gentian violet in water may be applied daily, and bichloride (1:10,000) or permanganate (1:5,000) packs or soaks may be prescribed. Mercury intolerance is common. Sulfathiazole, 0.5 gm. t.i.d., p.o., will control streptococcic complication. Penicillin 300,000 units in sesame oil injected intramuscularly each day is extremely efficient in secondarily infected dermatitis venenata. While it destroys cocci it does not promote active immunity, and its administration may be accompanied by a course of staphylococcus toxoid or undenatured bacterial antigen. Crude coal tar 2 per cent in lanolin will control seborrheic complication. If infection resists these efforts, foci of infection must be discovered and eradicated. The mouth must be freed of infection, and pyorrhea is as significant as a root abscess. We have cured many a case of chronically irritated and infected fingers by prostatic massage after elimination of oral infection failed to achieve the result. Onychomycosis likewise requires energetic attack in some cases. Seborrheic dermatitis of the scalp must be treated before the seborrheic complication of contact dermatitis of face, neck, or ears will yield.

**Ivy Poisoning.**—Severe reactions may follow the use of poison ivy antigen and large or frequent doses may prove dangerous although French and Halpin (AnnAllergy 1 131 1943) are among those who believe that injections of the alcoholic extract helped their patients. The Council on Pharmacy (J 1?? 91_ 1945) stated that treatment of the acute disease with ivy extract should be discouraged because many patients are made worse and no proof exists that any are helped. In our experience we have found other treatment preferable. Avoidance is by far the most satisfactory measure but hypersensitivity may be of remarkable degree and in such cases careful desensitization is worth trial. Shelmire's oral method is better, we think, than injections (ADS 44 983 1941). Locally some relief follows swabbing with per cent potassium permanganate solution and 1 cc boiled calamine lotion (Sompayrac AmJMSc 193 261 1939). *Prevention by use of 10 per cent sodium perborate in a protective ointment have succeeds* (Schwartz et al. PHRpt 57: 578, 194 ). Soap will remove some or all of the antigen only if used within 3 minutes of exposure and saturated aqueous KMnO may neutralize within 15 minutes, but no effective prophylactic exists in the opinion of Howell (ADS 45: 373 1943). One may scrub the blisters with gauze wet with alcohol then apply 10 per cent tannic acid for 20 to 30 minutes, repeating these measures as new blisters form with excellent relief though the face may not be so treated (Schwartz and Warren: PHRpts 56: 1039 1941). Our usual prescription calls for cool showers, cool aluminum acetate baths and compresses, carbolized calamine lotion, aspirin, and a barbiturate sedative. Greases must not be used, for they spread about on the skin any unattached allergen, which is fat soluble and which is normally got rid of mainly by exfoliation.

**Mustard Gas Burns.**—Prompt washing with green soap greatly reduces the severity of the lesions. If the chemical is allowed to remain on the skin, the burns are deep and severe although comparatively painless at first. One may immerse the injured part in Dakin's solution, the strength being about 0.5 per cent hypochlorous acid or weaker or use application of wet dressings saturated with the same solution. Dichloramine-T in chlorazone or chloramine-T in sodium stearate may be used. Greasy dressings are not good. One should cut off blister tops and paint the bases with gentian violet. Cl the 3 pped in l reced o l are protecti e

Tear Gas (CN) burns are treated with weak alkali washes. Diphenylchlorarsine (DA) is detoxified by chlorine water or KMnO.

## POMPHOLYX

**Symptoms.**—Pompholyx is a variously caused syndrome manifested by vesiculation of the thick epidermis of hands and feet. Vesicles characteristically appear in crops, are deeply seated and symmetrically located and usually affect the fingers and palms. At a given time the vesicles are of more or less the same size. Representative of epidermitis (q v ) and minute in their early development, they may progress in severity even to an extreme degree. The disease usually involutes without exudation after a few days and exfoliation follows, often taking the form of tiny expanding circular scaling lesions. Itching is intense during the active stage. Secondary infection may occur especially when salves are used in treatment. Recurrences are common.

Whatever the chemical may be that causes vesiculation of the thickest epidermis and the clinical syndrome of pompholyx, its prolonged and extreme effect when this occurs, is to damage thin epidermis also, so that there develop macular and edematous erythema and eczematous dermatitis which spreads symmetrically on the arms, the sides of the neck and face and the eyelids. The clinician would then give the disease a different name.

**Etiology.**—Pompholyx is a cutaneous reaction representing epithelial damage. Many cases are straightforward dermatitis venenata while others are dermatophytids, responsive to appropriate treatment. Feet and toenails, vaginal moniliasis, oral and prostatic focal infection account for some. Muende (BJD 46 479 1934) estimated that half the cases are

secondary to trichophytosis elsewhere. The lesions of pompholyx are free from parasites unless secondarily infected, and depend for their existence on deleterious chemicals directly contacted or absorbed from the metabolism of parasites located at a distance. Trichophytin or ragweed injections in overdosage may provoke attacks in sensitive persons. Hyperhidrotic individuals with psychosomatic difficulties are especially subject to pompholyx, of which not all cases are fully understood. In 7 selected psychoneurotic patients (Goldman MBullUCincinnati 8 79 1941) mecholyl injections provoked exacerbations while various other agents that act on the vegetative nervous system did not influence the disease



Fig. 44.—Pompholyx. Compare epidermophytid of Peck (ADS 2. 40 1930)

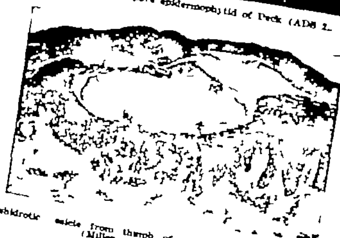


Fig. 47.—Dyshidrotic vesicle from thumb of patient with pedal dermatophytosis (Miller ADS 36 ... 1947)

Pompholyx-like eruptions were classified by Callaway and Barefoot (NCarolMJ 1 547, 1940) as (1) mycotic (2) allergic from contact fungi or bacteria, (3) idiopathic (4) toxic from food or drug (5) chronic infectious dermatitis, and (6) associated with general skin diseases. Becker (NebrSMJ 26 419 1941) attributed many cases to functional perversion of the sense of fatigue

**Diagnosis.**—The deep-seated vesicular character of the lesions, their symmetric distribution and their occurrence in crops are distinctive. Demonstrable parasites are absent. Elucidation of specific cause must be attempted in each case.

**Treatment.**—Rest, elimination of contactants, and symptomatic relief are essential. Mild, soothing astringents, such as cold compresses of 1:500 aqueous aluminum acetate or 1:5,000 potassium permanganate may be prescribed. Some patients obtain temporary relief by running extremely hot water over their hands. The lesions may be incised and drained. Suitable treatment must be directed against focal infection, mycotic or bacterial. Roentgen therapy is effective in fractional doses but must be prescribed with caution against overdosage.

## DRUG ERUPTIONS

**Symptoms.**—Dermatitis medicamentosa includes any eruption due to absorption of a chemical substance, particularly medicinal chemicals, differentiating contact dermatitis caused by medicinal agents. One must distinguish intoxication from intolerance. The latter comprises symptoms not normally produced by mere overdosage. Drug eruptions may simulate almost any dermatosis, and careful investigation is likely to be necessary to recognize puzzling cases. The lesions are likely to be widely and symmetrically distributed and of sudden onset and recurrence. Drug eruptions result from administration of chemicals by ingestion, injection, inhalation or inunction, or from absorption of them from their application to nasal, vaginal, anal, vesical or conjunctival mucosae or wounds, or through the pulmonary system, milk, or placenta. Sulzberger (Dermatologic Allergy) noted: Clinical manifestations include eruptions which are erythematous, morbilliform, scarlatiniform, eczematous, exfoliative, urticarial, purpuric, gangrenous, keratotic, vegetative, acneiform, furunculoid, dyshidrotic, hyperpigmentary or depigmentary, nodular or scleroderматous, or which simulate erythema multiforme, pityriasis rosea, lichen planus, herpes zoster, erysipelas, or lupus erythematosus. They may even include alopecia or pruritus without a rash.

**Etiology.**—The disease is usually accredited to idiosyncrasy, which may persist indefinitely. See classification of allergic phenomena, drug allergy, p. 30. Abramowitz (NYSJM 37: 128, 1937) reported that passive transfer is sometimes possible. Arsenical dermatitis may commence as Stokes and Kulchar (BJD 46: 134, 1934) noted at a dermatophytic focus.

The disease is not common. It occurred in about 1 of 2,000 patients seen at the University of Kansas Hospital (JKansMS 38: 385, 1937). The large majority, and by far the most serious cases, were those due to the arsenical antisyphilitic remedies, and the fatalities which occurred were among these.

Eruptions may be produced by minute amounts of drug although in most persons the drug provokes no rash even in large doses. Drug eruptions recur when the same or perhaps when a chemically related, substance is given. Identical eruptions may be provoked by dissimilar drugs. One drug may induce different manifestations in different persons. Specificity of drug sensitivity may be demonstrable. Some drugs experimentally sensitize human and other animal [illegible]. Drugs act like allergens in inducing diseases which exhibit incubation periods and subsequently altered reactivity to reexposure and [illegible] variations in host susceptibility are notable. Tuberculoid structure is rarely if ever produced, however. Reagin usually cannot be demonstrated. Eczematous eruptions may appear following internal administration of a drug after

contact dermatitis has been produced by it. Drug may produce photosensitization, vasomotor disturbances, nervous and visceral manifestations. Most proprietaries contain commonly intolerable drugs often more than one of such.

Arterial embolism when an oil emulsion is injected erroneously produces a typical syndrome of marmoraceous lividity soon followed by gangrene (Sulzberger and Baer: AmJS 41: 50 1940). Intravenous injection of such a medicine as bismuth subsalicylate in oil results in pulmonary embolism and death. Embolism following the use of sclerosing agent in treatment of varicose veins is rare (Sheller: J IL [illegible] 1939).

**Diagnosis** is established if the eruption disappears when the drug is discontinued and reappears if a small dose is given experimentally. Recognition is facilitated by suspicion, history and knowledge of the various potentialities of the disease.

**Treatment.**—Recognition of the cause and its elimination are essential. When one of several drugs might be the agent stop all of them. The wider the assortment of drugs a patient receives, the less the likelihood of catastrophe resulting from their withdrawal. If gastric lavage or catharsis will remove unabsorbed chemicals, it is indicated. BAL (p. 42) has utility in the metal poisonings, especially the arsenical ones. Silver pigmentation, arsenical keratoses, and severe arsenical dermatitis are becoming less common as wisdom in the use of medicines becomes more widespread. Overenthusiastic treatment of comparatively innocuous syphilitic infections, so that arsenical dermatitis results, has no justification. Permanent relief lies in complete avoidance of the provocative agent.

## TABULATION

**Acetanilide.**—Generalized erythema. Methemoglobinemia.

**Adrenalin.**—Urticaria, possibly from chlorobutanol (Rubin: J 135: 626 1945).

**Amidopyrine.**—Urticaria, neutropenia, bullae.

**Amphetamine Sulfate (Benzedrine).**—Rash (?) resembling atopic dermatitis.

**Androgenic Substances.**—Acneiform eruptions, hirsutism, enlargement of clitoris, diminution in size of breasts.

**Antipyrine.**—Usually morbilliform, may be urticarial, scarlatiniform, or even bullous. May involve mucous membranes. Moderate itching. Fixed eruption.

**Antitoxin.**—Immediate reactions: sweating, erythema, pruritus, urticaria, cough. Delayed reaction (accelerated serum disease) from 6 hours to 3 days. Serum sickness: urticaria, erythema, joint pains, malaise, fever, purpura, lymphadenitis, albuminuria, leukopenia. Anaphylactic gangrene.

**Arsenic.**—Erythematous, scarlatiniform, papular, vesicular, herpetic, urticarial, keratotic, pigmentary, ulcerative, even carcinomatous lesions. Palmar and plantar arsenical keratoses begin around the sweat follicles. Arsenical keratoses may improve under large doses of vitamin A (Hall: ADS 53: 154 1946). Arsenic trioxide produces an escharotic effect locally as well as erythema, weeping and scaling. Sensitivity to both trivalent and pentavalent arsenic may exist in one person. It is dangerous to give arsenic in any form to a patient sensitive to any arsenical. DAL yields remarkable improvement in all kinds of arsenical intoxication (Eagle and Magnuson: AmJS 30: 420 1946).

**Arsphenamine.**—Erythematous, scarlatiniform, morbilliform, and eczematous lesions followed by desquamation. Exfoliative dermatitis, beginning in the flexures of the extremities, then on trunk and head. Sudden erythema 9 days after injection. Purpura, hemorrhagic encephalitis, jaundice, hepatitis. Ulcerative colitis, perforation. Acute yellow atrophy. Agranulocytosis. Arsenical reactions of considerable severity may be expected perhaps once in 1,000 injections. Mapharsen is less toxic than other arsenicals and may be given to some patients even when previous intolerance has manifested itself, but if previously provoked dermatitis was severe no arsenical can be used without risking disaster (Levin and Keddie: J 119: 269 194?).

The value of the patch test in determining sensitivity to arsphenamine is controversial, but a positive test before its administration is a contraindication. Recognition of earliest lesion or other evidence of intolerance is fundamental in prevention of serious damage. Beerman and Stokes (AmJMSc 201: 611; 203: [illegible]) reviewed reaction and gave bibliography.



Fig. 88.—Arsenical keratoses. (Dr. Sa[illegible] S[illegible]ettler.)



Fig. 89.—Arsenical pigmentation. (Co[illegible] Drs. Forsyth and MacKee.)



Fig. 90.—Arsphenamine dermatitis with gangrene. (Ronchese, Am J S 13 [illegible] 1931.)

*Acidic Arsphenamine.*—Unneutralized arsphenamine given intravenously kills within a few minutes, as a rule.

*Nitritoid Reaction* occurs at once or within 10 minutes, and is characterized by suffusion of the face, sensations of asphyxia, even loss of consciousness. Epinephrine is the antidote. Serious reaction may be prevented by cautious injection. It is rarely fatal.

*Arsphenamine Collapse* occurs at once. It is rare. Abruptly the patient becomes pale, pulseless, and breathless, and experiences agonizing pain in the kidney region. Atropine is protective, 1/150 grain being given by hypodermic 20 minutes before injection.

*Shock* is rare following the administration of arsenicals. Weakness, cyanosis, cold skin, nausea, vomiting, collapse, syncope, fall in blood pressure, weakness and rapidity of the pulse, diminution of blood volume, rapid dehydration, increase in blood nitrogen, oliguria or even anuria occurring in progression. Not relieved by epinephrine, it may last for hours or days and is dangerous but unpredictable.

*Lichen Planus-Like and Pityriasis Rosea-Like Eruptions* may occur (Goodman and Sullivan: BMJ 36: 401, 1948).

*Nausea* and *Headache* frequently follow the injections. They are not contraindications to continuation of necessary treatment. Psychic influences are important in their cause and correction. At the time of injection, which should be given skilfully, the patient should not be hot, hasty, or exhausted, and he should have eaten a light carbohydrate meal perhaps two hours previously.

*Arsphenamine Dermatitis* is an absolute contraindication to the further administration of arsenic. It is presaged by itching and characterized by macular or blotchy, sometimes confluent, erythematous dermatitis, on the face, trunk, and extremities. The patient should be questioned *and examined* before each injection. Arsphenamine dermatitis is treated with BAL (p. 43) and by complete rest, soothing local applications, such as oatmeal baths or aluminum acetate (1:300) wet dressings, calamine lotion or Lassar paste, and sedatives such as aspirin. In the early stage sodium thiosulfate 1 gm. in 10 c.c. of water given each day intravenously may or may not be beneficial (Abramowitz et al.: ADS 47: 173, 1944). Epstein (J 100: 11, 1937) reported that all his patients with exfoliative dermatitis gave positive patch test reactions to neoarsphenamine. A course of heavy metal preceding arsenic seems to protect against the development of dermatitis but if given concurrently dermatitis is more likely to be severe. In 80 per cent the onset precedes the twelfth injection of arsenic. The recognition of itching palms, faint morbilliform rash in the antecubital areas, or itching or rash on the trunk, will prevent violent reactions or fatalities which would certainly follow the administration of more poison when mild symptoms of poisoning already exist. The occurrence of coincidental allergic dermatitis is indication that arsenicals should be temporarily discontinued. Furunculosis complicates many cases of arsenical dermatitis; this would not be so common if grease-free lotions instead of ointments were applied for topical relief, particularly in axillary and pubic regions. In treatment Epstein gave (1) 1,000 c.c. 10 per cent dextrose with 35 units of insulin intravenously daily; (2) one gram sodium thiosulfate intravenously on alternate days for 7 doses; (3) one gram calcium gluconate by mouth between meals t.i.d.; (4) four grams sodium bicarbonate by mouth t.i.d.; (5) colloid baths; and (6) a high protein diet. Symptomatic therapy including the administration of opiates when necessary may be devised for each case. Glucose and saline intravenously help combat severe toxicity. Liver extract for intramuscular administration seems helpful, especially if hepatic damage is in evidence. Atropine and vitamin C have been recommended.

*Erythema of the Ninth Day.*—Morbilliform erythema of sudden onset but generally innocuous nature sometimes appears about the ninth day after a dose of arsphenamine. The rash appears on the trunk and limbs, spreads to involve the whole body, reaches its height in 24 to 48 hours, disappears usually within 3 or 4 days. It is accompanied by general lymphadenopathy and variable constitutional symptoms, including fever which falls when the eruption fades (Epstein and Levin: AmJS 23: 490, 1939). While considered by some to be not a contraindication to further treatment, 14 cases of ninth day erythema in which arsenical treatment was promptly resumed suffered severe parenchymatous injury, reported Leifer (AmJMSc 210: 458, 1945).

*Hemorrhagic Encephalitis* occurs perhaps once in 3,000 patients on routine therapy, usually after the second dose; the onset is within 1 to 144 hours after the dose with headache, vomiting, chills, fever, cyanosis, convulsions, coma, loss of sphincter control, mental changes, stiff neck, neurologic signs of encephalomyelitis. Death is the usual outcome. Pregnant women comprised 70 per cent of 158 cases collected by Paley and Plewett (AmJS 23: 68, 1939). Massive dose and intensive methods have in the past carried a mortality approximating 1 per cent from this dread complication, wherein congestion, edema, focal necrosis, and capillary hemorrhages damage the central nervous

system sometimes irreversibly (Boyd and Nie: ANeurP 49 863 1943). If recognized early by alert personnel, however BAL (p. 4 ) successfully detoxifies (Eagle and Magnuson: AmJS 30: 420 1946). Other therapy includes posture (the sitting position) administration of fluid and plasma decompression by repeated lumbar puncture control of hyperpyrexia and sedation with paraldehyde (Ransome et al. BMJ 1: 639 1945).

*Agranulocytosis.*—Neutropenia is the first detectable symptom of agranulocytosis due to arsenicals. BAL, repeated transfusions, and penicillin are the hope here.

*Jaundice.*—Impairment of liver function and significant drop in prothrombin indicate arsenical intoxication, yet discontinuation of treatment when these occur may not succeed in preventing serious complications and vitamin B, C, or K, or liver extract neither prevent nor protect so that massive arsenotherapy should be abolished, according to Hind and Kalz (AmJS 30: 70 1946). The incidence and severity of hepatitis are not related to the total amount of arsenic given, and histologic distinction cannot be made from epidemic or postserum hepatitis, wrote Dibble and McMichael (BJVD 19 102, 1943). Jaundice in syphilis thought due to arsenicals probably actually is infective jaundice transmitted by faulty aseptic technic in treatment in many instances (Marshall: BJVD 19 5 1943) although arsenical toxic hepatitis of course does occur and may be fatal.

**Aspirin.**—Erythematous papular at times hemorrhagic. Urticaria, edema, asthma. Purpura. (Ed t. J 116 14 1941.)

**Atabrine.**—See Quinacrine.

**Atropine.**—Erythematous scarlatiniform. Eruption patchy or generalized, usually itching sometimes tenderly so. Pyrexia convulsions.

**BAL.**—Intoxication, cramps tetany (Salzberger et al.: JClinInv 25: 4 4, 1946).

**Benadryl.**—Drowsiness nervousness dryness of upper respiratory passages, weakness, fatigue ataxia, facial edema, nausea tinnitus pruritus hysterical reaction, stupor confusion, sore tongue exhaustion, collapse headache shock (Geiger et al.: J 133 39 194 ). Urticaria purpura (Dennie).

**Barbiturates.**—Exanthema with fever. Urticarial, erythematous, bullous, and serous eczematous or fixed eruptions. Pruritus purpura, leucopenia, photosensitization. Exfoliative dermatitis (Wiener and Bae: ADS 43 4 3 1941); stomatitis and conjunctivitis (Moss and Long: ADS 46 336, 194 ); see Novy (CalifWM 43: 324 1939).

**Benzedrine.**—See Amphetamine.

**Bismuth.**—Pigmentation of gums, ulcerative stomatitis, erythroderma, papulosquamous erythema, scarlatiniform erythema, urticaria, and pruritus. Embolism, nephritis, agranulocytosis ulcerative colitis argyria-like pigmentation arthralgia, jaundice. Brittingham (JMAGa 22 323 1933) showed that stomatitis is of high incidence in persons with caries or pyorrhea. Salivation pain and swelling of tongue gastric upset with watery diarrhea and griping, renal irritation with frequency weakness, malaise, albuminuria (even anuria) headache backache and malaise similar to influenzal symptoms excepting the lower fever—all these occur in bismuth poisoning. Ninth day erythema (Grund: ADS 41 10 6 1940).

**Bromides.**—Fairly common present in some headache remedies. Lesions develop slowly and are persistent. Erythematous pustular urticarial, furuncular condylomaform, bullous, and squamous. Eruption localized or general. Hemorrhagic fungating lesions, erythema nodosum-like toxic psychoses common. Treat by urging quantities of sodium chloride and water and sodium chloride solution intravenously or by intravenous sodium chloride solution continuously by drip, with continuous suction of gastric juice from the stomach. No relation between blood bromide level and skin lesions (DeGowin: J 113 466 1939).

**Chloral Hydrate.**—Papular lichenoid urticarial, purpuric erythematous and scarlatiniform. Frequently small bullous.

**Chloroform.**—Erythematous or purpuric.

**Cinchophen.**—Angioneurotic edema erysipelatous swelling of face, pruritus, scarlatiniform rashes jaundice death.

**Cod-Liver Oil.**—Acne form. Excessive amount of substances rich in butter fat (cream, for example) has similar effect.

**Codeine.**—Exanthema with pruritus sometimes follicular or perifollicular and scarlatiniform (Feldman: ADS 4 654 1943).

**Cyverine.**—This antispasmodic has apparently caused alopecia.

**DDT.**—Dermatitis and flexural erythema, papules, and purpura (Striker and Godfrey: JMoSMA 43 354 1946).

**Diasone.**—Red macular papular rash with enanthem, becoming vesicular (Pfeifer and Pyle: J 1-3 334, 1944).

**Digitalis.**—Erythematous and papular followed by desquamation.

**Dinitrophenol.**—Urticaria purpura, pruritus, acroerythema.

**Diodrast.**—Urticaria and wheezing, from intravenous pyelography

**Diphenylhydantoin Sodium** (Dilantin, Phenytoin Sodium).—Pruritic scarlatiniform eruption, hemorrhagic erythema multiforme (Ritchie and Kolb: ADS 46: 856, 194.) Bullous pluriorificial dermatitis (Ellis BMJ 36 575 1943)

**Epinephrine.**—Local gangrene (Cohen and Waterston JAllergy 11 393, 1940)

**Ephedrine.**—Pompholyx. Eczematous dermatitis.

**Ergot.**—From ergoted grain or ergotamine tartrate. Ischemia and gangrene. Papaverine is antidote (Loe N WM 47: 190 1948.)



Fig. 31.—Barbiturate dermatitis due to luminal Miliary, morbilliform, generalized (Courtesy of Drs. Fordyce and MacKee.)



Fig. 32.—Arterial embolism following accidental injection of bismuth in oil into the inferior gluteal artery Left to right Dry gangrene and beginning separation of slough on 15th day spontaneous separation of slough, followed by granulation and partial healing, seen on 49th day foot drop present the scar many months later (DeWolf UCalRev 37 423 1933.)



Fig. 93.



Fig. 94.

Fig. 93.—Bromide eruption. (Dr F Ronchese.)
Fig. 94.—Bromide eruption, vegetative, in epileptic patient.

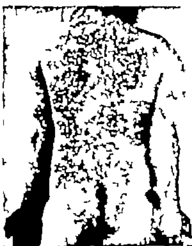


Fig. 95.



Fig. 96.

Fig. 95.—Dermatitis medicamentosa from copaiba. (Dr A J Markley.)
Fig. 96.—Purpuric iodide eruption in nursing infant whose mother took iodide. (Dr D Wood Ruggles.)

**Estrogen.**—Purpura (Watson et al. JLCM 32: 606, 1947)

**Fixed Eruptions.**—Erythematous, swollen, and bullous plaques followed by pigmentation, suddenly recurrent in the same places with each dose of the drug have resulted from antipyrine phenolphthalein, barbiturates, cinchophen, mercury quinine, acriflavine acetylarsan Mapharsen, Tryparsamide Early the eruption is urticarial, eczematous, and pruritic. (Abramowitz: ADS 43: 672, 1941)

**Frei Antigen.**—Papular eruption. Fever Erythema nodosum.

**Gold.**—Gold sodium thiosulfate and gold inside Sanocrysin, may produce erythema, morbilliform eruptions, alopecia, stomatitis, exfoliative dermatitis, urticaria, and purpura. BAL cures (Cohen: J 133 749 1947) Argyria-like pigmentation (chrysocyanosis) especially about eyes. Pityriasis rosea-like (Wile and Courville: ADS 4 1103, 1940)

**Hexamethylenamine.**—Urticaria, erythema.

**Insulin.**—Urticaria, and sometimes the clinical picture of serum sickness. Lipoma-like hypertrophy or atrophy at site of injection.

**Iodides.**—Erythematous purpuric urticarial acneform, papular nodular pustular bullous, carbuncular and vegetating. Fatal hemorrhagic vegetative, and ulcerative dermatitis. Lachrymation, salivation red nose Sites of predilection are areas richest in sebaceous glands—face shoulders and back—although no region is exempt The lesions may be discrete or confluent, and there may occur suppuration and ulceration, eventually scarring The eruption generally appears promptly within 24 or 48 hours, but it is usually persistent. Intravenous sodium thiosulfate checks reaction from potassium iodide given orally to an iodine-sensitive person. Persons with cardiac or renal embarrassment are susceptible (Wartski: MJAustral : 738, 1933)

**Iodoform.**—Macular purpuric, papular, vesicular

**Karaya Gum.**—Urticaria (Bowen: ADS 39: 506, 1939) Used in some laxatives, gum drops, hand and hair lotions.

**Lipiodol.**—Iodism; see Iodides.

**Liver Extracts.**—Erythema, urticaria asthma (Feinberg et al. AnnIntM 18 311 1943)

**Mercury.**—Erythematous and scarlatiniform, occasionally followed by desquamation. Tattoo and pigmentation Salivation and stomatitis.

**Mesantoin.**—Methyl phenyl-ethyl hydantoin caused macular rash, fever eosinophilia, agranulocytosis. Bullous, fatal case of Roskin (J 137 1031, 1948)

**Morphine.**—Erythematous, maculopapular vesicular urticarial. Pruritus.

**Nicotinic Acid.**—Transient vasodilatation, flushing itching urticaria. Dizziness, nausea, vomiting.

**Penicillin.**—Reaction resembling serum sickness (Gordon J 131 727 1946) Vesiculation with or without spreading scarlatiniform eruption of toes, feet crotch (Lamb ADS 52 93 1945) Pompholyx. Herxheimer-like phenomena, and aggravation of bacterid (Heinlein et al: USNMBull, April, 1946) Oral administration frequently provokes urticaria. Universal erythema perhaps with dependent petechiae. Erythema multiforme-like eruption, preceding from the dermatosis for which penicillin was administered. Erythema nodosum with superimposed bullae. Dermographia without urticaria (Kalz: ADS 54: 66, 1946) Exfoliative dermatitis (Nolan and Pedigo: AnnIntM 23 72, 1936) Pityriasis rosea-like (Epstein J 134 733, 1947) Agranulocytosis (Spain and Clark AnIntM 25 732, 1946) Topical application: eczematous dermatitis; flares of this may occur if subsequently penicillin is given parenterally (Templeton et al. ADS 56 323 1947) Angioneurotic death have occurred (Wile 1946) Sensitization related to *T. gypseum* infection (Cormia and Lewis JInvD 7: 375, 1946); not related (Peck and Siegel ib. 9 165 1947) Passive transfer test negative in penicillin urticaria (Callaway and Barefoot; JInvD 7 253 1946) Reaction rate about 9 per cent, commonest urticaria epidermal sensitization easy to induce (Gottschalk and Weiss ADS 53 4 1946) Classification of reactions, see Farrington et al. (SMJ 41 614 1948) Exfoliative dermatitis (Shaffer: NEngJM 238 660 1948) Spontaneous sensitivity in 5 per cent; 10 per cent of those receiving penicillin got reactions, mostly males probably due to previous therapy (Peck et al.: J 138 631 1948)

**Phenacetin.**—Urticaria erythema.

**Phenolphthalein.**—Persistent spots first pink and then becoming purplish or brownish; fixed eruption. Feenamint Ex Lax, Agarol common in histories. The unbroken molecule is the cause Bullae stomatitis, catarrhal colitis. (Abramowitz: ADS 40 434, 1938)

**Pituitary Posterior.**—Urticaria (McMann J 113 1488 1939)

**Prontosil.**—A sulfonamide q.v



Fig. 97 —Iodide eruption, bullous, hemorrhagic and fatal, due to lipiodol. (Goldstein J 106 1039 1936.)



Fig 98 —Phenolphthalein eruption. (Dr Bedford Shelmire.)

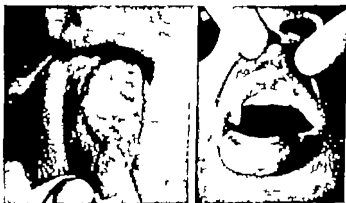


Fig. 99. Fig. 100.

Fig. 99.—Phenolphthalein glossitis. (Dr Bedford Shelmire.)
Fig. 100.—Phenolphthalein cheilitis (Dr Bedford Shelmire.)

**Quinacrine (Atabrine).**—Yellow pigmentation usually general but more intense on exposed parts (Sugar and Waddell: JAMA 80: 224, 1946). Blue macules on face, nose and mucosae. Blue nails (Sugar and Waddell: Bull U.S.A.M.D. 4: 370, 1945). See lichen planus p. 513.

**Quinidine.**—Edema; scarlatiniform, pruritic, general or scattered, often dependent. Purpura (Nodelman et al.: J. 137: 1: 19, 1948).

**Quinine.**—Erythematous, scarlatiniform, purpuric, urticarial, vesicular, bullous, and ulcerative, attended with severe itching.

**Radium.**—Destruction of mandibles; sarcoma. (J. 11: 1833, 1939.)

**Rutin.**—Conjunctival petechiae (Wolffe and Dunlap: J. 134: 602, 1947).

**Salicylates.**—Erythematous, scarlatiniform, morbilliform, urticarial, vesicular, bullous, and, rarely, ulcerative. Thrombocytopenia.

**Sclerosing Agents.**—Emboli are less common since coagulants are less used. Sodium salicylate may cause urticaria. Quinine (q.v.). Sodium morrhuate (q.v.).

**Sedormid.**—Thrombocytopenic purpura.

**Selenium.**—Erythema and edema of exposed parts, porphyria and leucocytosis with relative lymphocytosis (Halter: abs. YBD 1939 p. 46).

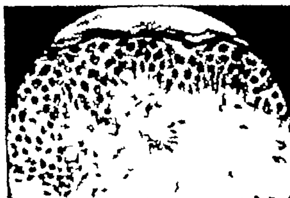


Fig. 101.—Argyria: pigment in epidermis and dermis in finely disseminated particles. (Dr. Stuart C. Way.)

**Silver.**—*Argyria is permanent discoloration of the skin which sometimes follows* prolonged administration of silver salts, particularly silver nitrate. May result from use of Argyrol or silver arsphenamine. Earliest signs of pigmentation are noted on the edges of the gums. The hue of the affected skin ranges from a bluish or bluish gray to a slate or bronze color. May be generalized or localized to treated area. The deposit of silver or rather the silver combination is limited to the margin of the connective tissue and affects particularly the elastic fibers and the sheaths of the membranes (Hill and Montgomery: ADS 44: 588, 1941). Many elastic fibers are sheathed with the metal. Hilliard and Lawless (J. 93: 20, 1929) successfully bleached the pigmentation by injecting locally a mixture of 1 per cent potassium ferricyanide with 6 per cent sodium thiosulfate.

**Sodium Morrhuate.**—Pruritus, erythema, edema, flare at sites of previous injections. Urticaria, collapse. Embolism (Shelley: J. 11: 1792, 1939.)

**Stilbestrol.**—Edema of legs; erythema progressing to exfoliative dermatitis (Keyser: YaleMonth 60: 11: 104; Kesselberg: J. 120: 117, 1942).

**Streptomycin.**—Histamine-like flushing, headache, fever, myalgia, and arthralgia. Maculopapular and erythema nodosum-like exanthems (Hettig and Adcock: Sc. 103: 355, 1946). Rashes resembling erythema of ninth day not a contraindication to further dosage (Strauss and Fishbein: ADS 56: 711, 1947). Contact dermatitis (Strauss and Warring: JI U.S. 3: 99, 1947). Severe membranous stomatitis.

**Sulfonamides.**—Erythema with edema, urticarial, followed by desquamation. Scarlatiniform. Tends to localize on parts exposed to sunlight: photosensitization. Erythroderma. Pruritus, granulopenia, purpura. Cyanosis. Methemoglobinemia. Porphyrinuria. Acute yellow atrophy. Headache, nausea, vomiting; worse with sulfapyridine. Erythema nodosum-like eruptions. Exacerbation flare of exudative dermatitis for which drug was given with development of widespread eruption more



Fig. 102.—Sulfapyridine eruption confluent on exposed parts. (Thompson BMJ 2 12, 1939.)

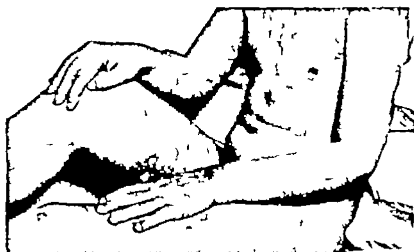


Fig. 103.—Sulfonamide eruption which appeared on 8th day of administration of drug. Photograph on 10th day. (Thompson BMJ 2 12, 1939.)



Fig. 104.—Pemphigoid sulfonamide eruption. (Bloom NYSJM 42 1499 1942.)

or less resembling the original disease (Livingood and Pillsbury: J 121: 406, 1943) Conjunctiviti and fever Pemphigoid eruption (Johnson: J 1-4: 979 1944) Fixed eruption (Dostrovski and Sagher ADS 49: 418, 1944) General erythema, conjunctivitis, and purpura, fatal (Gessler: BMJ 2: 863, 1944) Peripheral neuriti Anuria. Topical use often sensitizes, so that subsequent internal administration causes sensitization phenomena of any kind especially local flare (Tulloch: BMJ 2: 313, 1943 Shaffer et al.: J 123 17 1943) Percutaneous absorption can cause any toxic phenomenon that oral administration can (Peterkin BMJ 2 1, 1945) Sensitization from sulfonamide medication is flared by contact with sulfonamide resins such as nail lacquer may contain. Treatment of sulfonamide intoxication: para aminobenzoic acid, r chemically r lated procaine 1 per cent 5 c.c. subcutaneously each 4 hours (Dixon Pers comm. 1943) If patch test i positive oral testing i hazardous (Phillips BJD 58 ?13 1946) Contact sensitization is more likely to develop if skin is inflamed experimental sensitization by Gottschalk and Weiss (ADS 56 775 1947)

**Testosterone.**—See Androgen

**Thallium.**—Alopecia, nephritis, formication in hand and feet, encephalitis, arthralgia, gastrointestinal pain anorexia, insomnia, th rst, depression. Treat with sodium thiosulfate and vitamin $B_1$. Try BAL.

**Theelin.**—Erythema at sit of injection, spreading to become general.

**Thiamine.**—Angioneurotic edema (Eisenstadt: MinnM 25 861 194.) Macular itchy erythema.

**Thiocyanate.**—Macula , maculopapular dermatitis. Itching and scaling. Exfoliative dermatiti s. See Watkinson and Evans (BMJ 1 303, 1947) Urticaria (Wald et al.: J 11 1120 1939

**Thiouracil and Thiourea.**—Morbilliform eruption fever Erythematous macular papular acneform rashes. Pruritus. Edema of legs. (VanWinkle et al. J 130; 343, 1946.) Urticaria, neuritis arthritis, malaise (Williams JClEndocr 6 23, 1946) Thrombocytopenic purpura.

**Tridione.**—Purpura, aplastic anemia (Harrison et al J 132 11 1946)

**Tryparsamide.**—Optic atrophy Urticaria, eczematoid fixed eruption.

**Tuberculin.**—Erythema, urticaria, erythema nodosum. Local reaction mild severe even sloughing. Tuberculid.

**Vaccines and Bacterins.**—Erythema, papular and urticarial rashes Erythema multiforme

**Vitamin D.**—Exudative conjunctiviti nausea, weakness, coma, peripheral and optic neuritis; nonfatal (Macrae BJD 60 33, 194 ) See p. 1..

## URTICARIA

**Symptoms.**—Urticaria (nettle rash, or hives) is an inflammatory affection characterized by the eruption of whitish, pinkish or reddish wheals, caused by transudation of fluid from vessels into tissue spaces in allergic response to the local release of a histamine-like substance. The lesions are evanescent and give rise to burning itching and stinging sensations. Wheals vary greatly in size and considerably in shape. They usually appear suddenly They are elevations, pinhead to fingernail-sized at first, but frequently they coalesce to form irregular patches. Rarely they become purpuric and are followed by temporary pigmentation. Any or all parts of the body may be affected, but the sites of predilection are the lower trunk, buttocks, and outer surfaces of the thighs. In ordinary cases the lesions persist for several hours and then disappear spontaneously leaving no trace. Rubbing usually renders the lesions worse instead of better and may provoke a new outbreak in regions previously unaffected. The mucous membranes notably those of the larynx, may also be involved

Dermographism is characterized by the provokability of linear wheals by one s simply rubbing or stroking the skin with some pointed instrument Walzer (ADS 37 659 1928) demonstrated passive transfer of dermographia inducing factors in 7 of 12 persons tested.

Black dermographism is a physical phenomenon dependent on powder present on the skin. When the skin is stroked with certain metals, particles scraped off leave their mark. The same reaction may be obtained on paper, cloth and wood, reported Urbach and Pillsbury (J 121 480 1943). This has nothing to do with urticaria or dermographia.

ACUTE URTICARIA is the most common clinical type, an attack extending over a period of 3 or 4 days. During this time crops of new lesions are constantly appearing after older ones have subsided. The disease may then disappear permanently or it may recur.



Fig. 105.



Fig. 106.

Fig. 105.—Urticaria, showing ordinary and giant wheals.
Fig. 106.—Urticaria, severe and confluent acute attack. (Dr. Otto L. Castle.)



Fig. 107.—Dermographism.



Fig. 108.—Angioneurotic edema.

Chronic Urticaria may consist simply of repeated attacks of acute urticaria extending over a period of months or even years. Or the individual may have lesions continuously with or without exacerbations.

Papular Urticaria (Lichen Urticatus) —The lesions are papular and yet possess some of the characteristics of wheals. They are pinhead to pea-sized, flat sharply defined, and intensely itchy and are usually comparatively few in number This type is observed most frequently in poorly nourished children, although adults are not immune. The loins and buttocks are the sites of predilection. Cole reported a case in a Negro cured

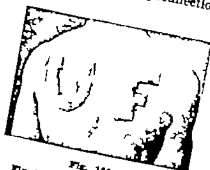


Fig. 109



Fig. 110.

Fig. 109—Urticaria elicited by mechanical irritation. Edema does not extend beyond the skin area directly irritated. (Dr W W Duke.)

Fig. 110.—Urticaria elicited by light. The area of edema does not extend beyond the area directly exposed to light (Dr W W Duke.)

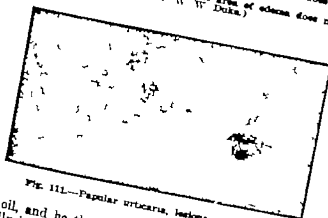


Fig. 111.—Papular urticaria, lesions on abdomen.

by cod-liver oil, and he thought it a manifestation of avitaminosis. Patients generally improve in hospital even when their food is brought from home Pillsbury and Sternberg (AmJDisChild 53 1209 1937) reported good results in 85 per cent of their cases which were treated with calcium and parathyroid extract and similar results in 38 per cent of those treated by calcium alone. Clinical improvement seemed chiefly concerned with the elevation of the level of the calcium content of the blood. They thought that evidence supporting a view of allergy as the cause of papular urticaria is meager Ellis (BMJ 2 118 1942) recommended potassium citrate 10 grams t.i.d by mouth. It has been suggested that the cause may be external, and that bedbugs or fleas may play a part.

Serum Sickness presents urticaria as one of its major symptoms. Its phenomena are thought to be due to release of the H-substance from the union of serum protein antigens and antibodies. Histaminase (Best and McHenry JPhys 70 349 1930) has helped many patients (Foshay and Hagebusch J 112 2398, 1939) and failed in others. The antihistaminic substances such as Pyribenzamine are quite effective in palliating the urticarial element but influence the arthralgia little.

Angioneurotic Edema is a form of urticaria characterized by large, single or multiple circumscribed, evanescent edematous swellings. The lesions differ from urticaria only in size. The regions commonly involved are the lips, the eyelids, and the lobes of the ears, although the extremities, trunk, larynx, and genitals occasionally are involved. The lesions are somewhat more persistent than those seen in urticaria. The disease is sometimes familial (Fineman AnnIntM 14 916, 1940). Kafka (MRec 146 441, 1937) recommended ephedrine sulfate, gr ¾ by mouth, and starch-water baths. In edema of the glottis, he found effective the repeated administration of adrenalin at intervals of ½, 1, 2, 4 and 8 hours. It is in these cases that a tracheal catheter or as a last resort tracheotomy may be required. Antihistamine drugs are effective.

**Etiology of Urticaria.**—Increased blood capillary permeability is concerned, or else diminished lymph capillary resorption, perhaps both. The injection of histamine evokes a wheal. (See p 28 and p 30.) An attack of urticaria occasionally follows the ingestion of a particular food or drug. Allergy may be of obscure origin, in some instances multiple factors being involved. In some cases urticaria can be brought on by the specific action of physical agents (see p. 31) such as light, heat, cold, scratching and in heat sensitiveness by either mental or physical exertion. *Attacks may be precipitated by the ingestion or parenteral introduction* of foreign proteins, especially serums and bacterial products. Menstrual urticaria is believed to be due to some secretion occurring in the blood during the menstrual period. The psychic factor in the etiology of certain types of the disorder was reviewed by Stokes et al. (ADS 31 470 1935). They attributed 10 per cent of the cases of chronic urticaria to this. Serum calcium estimations, studied by Greenbaum (ADS 16 553 1927) in 63 patients representing all forms of urticaria showed a normal or increased calcium level. He concluded that the administration of calcium salts to patients with urticaria generally lacks scientific basis. Increase of serum potassium during activity and diminution thereof during decline of urticaria, as is true also in asthma, was described by Rusk et al (J 112 2395 1939). Patients with urticaria who had low prothrombin levels were often relieved by vitamin K, 2 mg t.i.d. before meals (Black JAllergy 16 83 1945). Cases associated with disease of the biliary tract and favorably influenced by cholagogues and biliary drainage were reported by Menagh (J 90 668, 1928). Inhalants, such as ragweed pollen may cause urticaria as they cause asthma (Derbes and Englehardt SMJ 37 729 1944).

Hopkins and Kesten (ADS 29 358 1934) were able to demonstrate the etiologic factor in many cases, although some could not be ascribed to a known cause. They classified provoked causative agents as follows:

I Acute Urticaria (single or repeated attack.)
  A Localized.
    1. Plant, insect, jellyfish poisons.
    2. Contact substances to which skin is sensitized.
    3. Heat, cold, light, mechanical irritation. (Many agents producing generalized urticaria may produce it locally.)

B. Generalized.
4. Serum sickness anaphylactic shock.
5. Food
6. Foreign substances absorbed through conjunctiva or respiratory tract.
7 Drugs.
8. Heat (exertion, excitement, fever)
9 Infections.
10. Menstruation.

II. Chronic Urticaria.
11 Food (rarely)
1.. Focal infection (frequently)
13. Animal parasites.

Etiologic grouping of 170 cases by Fisk and Gay (BullJHH 53: 280 1934) was as follows

1. Foci of infection, 30 per cent. Of these 74 per cent were cured by elimination of the focus.
2. Allergy to food, drug external agent, scabies, 20 per cent.
3. Psychogenic 18 per cent.
4. Endocrine 5 per cent. All were females.
5. Unknown 23 per cent.

Urticarial trichophytids occur Many animal parasites, includi g *Schistosoma japonicum* may cause urticaria. The lack of vitamin C must be considered. Chronic cases are usually due to foods, according to Kahn and Grothaus (NMJ 33 1086 1940) Women are more often affected than men.

**Pathology**—A wheal is an acute, inflammatory edematous lesion due to the action of a toxic agent which may reach the dermis from within or from without. Changes occur in papillary and subpapillary regions of the dermis and consist in vascular dilation with profuse outpouring of serum and white cells. The dilated vessels are filled with leucocytes. Throughout the affected area perivascular infiltration is a prominent feature. Lesions may occur in the gastrointestinal tract.

**Diagnosis.**—Wheals are distinctive When urticaria has been recognized, the diagnostic problem has begun, not ended

**Prognosis.**—An ordinary attack of urticaria is self limited, and the lesions shortly disappear spontaneously Chronic urticaria usually proves a vexing tedious problem.

**Treatment.**—In the acute cases, while a strange or unusual food may be the provocative factor some simple article of diet may be the principal offender and it is only after suffering from repeated attacks that the patient may be able to recognize his idiosyncrasy Usually a cathartic is necessary and a saline best serves the purpose It may be given routinely at the outset in acute cases.

Chronic recurrent urticaria sometimes taxes the resources of the medical attendant to the utmost Careful search should be made for causative factors. The possibility of parasitic infection must be eliminated. Internal medication capable of causing urticaria must be discontinued. Suspected external allergens must be eliminated. Focal infection should be sought to be attacked later if necessary Indications of endocrine imbalance especially thyroid, are pertinent The presence of emotional instability should be noted. Inhalant allergens must be removed or determined and adequately treated. Detection of ingested allergens must be achieved although histamine desensitization may be tried, giving tiny doses at first, or antihistamine (Benadryl, Pyribenzamine) palli tion prescribed. Histaminase may be given by mouth in f

coated capsules, 2 or more tablets each 2 hours sometimes with good effect, on the hypothesis that urticaria is due to histamine and that the ingestion of the histaminase does away with it In 35 cases, Laymon (MinnM 25 466 1942) reported 21 cures with daily doses varying from 60 to 120 histamine detoxifying units

When we assume control of a patient with urticaria acute or chronic, we consider the etiologic possibilities listed above, order a saline laxative, and prescribe (1) Pyribenzamine 50 mg each 8 hours and (2) limitation of ingesta for 24 hours to water and rice cooked in water salted and sugared to taste. The patient is almost invariably much improved when seen the next day Thereafter we may continue with the detection of food allergens after the effective method devised by Winston and Sutton (Pract 160 347 1948) A single simple food, not a mixture of foods, is tested by eating it and waiting until the following meal to see if it has caused urticaria. Water cane sugar and noniodized salt are permitted freely and rice oatmeal beef beets, milk, and bread are tested at successive meals A food that has been tested and is not followed by urticaria may thereafter be eaten right along. Thus, the number of foods which may be selected for the next meal rapidly increases When urticaria follows the eating of a food, that food is tentatively considered to be an allergen and is not eaten again for one week. If urticaria follows a food upon retesting it is considered proved to be an allergen No new food is tested until the urticaria subsides. An antihistaminic of the tripelennamine hydrochloride type may be given to suppress the urticaria that may develop The patient is given daily a list of the foods tolerated, those suspected upon initial testing those proved causative upon retesting and the new foods to be tested. This method, in contrast to skin testing tests foods by eating them in the manner in which they are normally encountered The specific ingested allergen is identified with precision avoiding the uncertainty of the multiple choice elimination diets The use of undiluted food extracts for skin testing and the elimination of all positively reacting food items was recommended by Kahn and Grothaus (SMJ 33 1086 1940)

Of the internal remedies the senior author has found a cascara and bile salt preparation valuable A pancreatic extract lacking insulin (Depancol for example) may relieve at least while it is being given (Markel ADS 39 992 1939) Calcium is commended by some but not by us. Epinephrine is best given in small doses of 0.2 to 0.3 c c of the 1 1 000 dilution, repeated each half hour or hour until relief is obtained. Ephedrine often proves helpful. Wise (YBD 1936 p 6) recommended pilocarpine in 1 per cent aqueous solution giving 3 drops first and increasing to 20 drops t.i.d. trying atropine later if this fails. The injection of a foreign protein, such as typhoid bacterin, sometimes proves beneficial (Traut ADS 40 368, 1939) Dilute hydrochloric acid, 30 drops t i d with water often helps. Nicotinic acid is claimed to have cured some cases and to have caused others

Antihistamine preparations such as Benadryl and Pyribenzamine frequently afford valuable palliation (see p 42) They are taken orally in doses of 25 to 100 mg at regular intervals of from 4 to 12 hours. Some patients prefer hives to the all in feeling some of these drugs may produce, but others are completely relieved.

Chronic urticaria was attacked by Burgess (BMJ 1 662, 1939) by a program which included elimination of focal infection, elimination of

foods to which the patient is sensitive investigation of psychologic troubles, treatment of dyspepsia with hydrochloric acid, the administration of glucose and calcium, and some method of desensitization such as autohemotherapy

Local applications which may alleviate the itching include (1) carbolized calamine lotion with or without 1 to 3 per cent of alcoholic solution of coal tar (2) saturated aqueous solution of sodium carbonate or bicarbonate or of borax, (3) isotonic baths of sodium chloride, ammonium chloride or magnesium sulfate and (4) applications of vinegar Salves are not satisfactory Medicated soap woolen garments, and irritating local applications are among the things to be avoided. The relief of fatigue and irritability is usually important. Interdiction of coffee and the administration of aspirin are serviceable measures. Some patients find no lasting relief despite every effort.

## FOREIGN BODY GRANULOMAS

The responses of tissues to chemical substances gaining access to them in various ways are of basic interest in the comprehension of *inflammation (q v., p 20) A number of cutaneous lesions depend on* such phenomena.

TISSUE REACTIONS TO LIPOIDS.—Reactions to olive oil and cod-liver oil and their fractions were investigated by Hass (APath 26 936 1938) Reaction to the whole oil was mild with olive oil, and some of it remained in situ unchanged after 3 weeks. With cod-liver oil, however the reaction was inflammatory and none remained unaltered in situ after 3 weeks. The glycerol fractions provoked little reaction but fractions of cod-liver oil were more irritating than those of olive oil. Nonsaponifiable fractions caused severe reaction and sloughs resulted unless the dose was kept small; destruction resulted mainly from the alcohol-soluble compounds of the nonsaponifiable *fractions of both oils. Fatty acids provoked the most intense reactions* of the lot, and those from cod live  il were more irritating than those from olive oil Reactions to methyl esters of *saturated* acids were comparatively mild, for the material was rapidly hydrolyzed in the intercellular environment, acid crystals appeared in the zone and giant cells applied themselves to these foreign bodies. To methyl esters of unsaturated acids of cod liver oil, the reactions were more intense and there formed in the intercellular regions quantities of semisolid amorphous matter which served as a potent stimulus to the formation of giant cells. *I tensity of inflammatory response increased with increase in average unsaturation* of the lipoid fraction tested. Epithelium partook of the reaction, for cysts developed a a defense mechanism, deriving demonstrably at times from the epidermis or from the accessory structures, so a to enclose, by surrounding from above the fibrous zone of connective tissue reaction.

When unassimilable substances are i jected, there occurs early an influx of polymorphonuclear leucocytes, which subsides in a few days (Tompkins AmJS 20 22, 1936) Monocytes appear the th rd day after the injections; they enlarge and become more active Clasmatocytes appear in 5 days then epithelioid and transitional forms w thin 8 days. Giant cells of foreign body and epithelioid types are present after about 10 days. When lecithin, which is assimilable is injected, focal increase in macrophages occurs but degenerative changes do not, and epithelioid and giant cells do not appear Assimilable lipoids are removed from zones without residual modification of the tissues.

Reactions to fractions isolated from tubercle bacilli were described by Sabin (PhysRev 1. 141 1932 see also p. 210) The phosphatid fraction is phagocytosed by monocytes, *degrades them, and provokes tubercle formation.* The unsaponifiable waxes stimulate the production of undifferentiated connective tissue irritate and call forth leucocyte infiltration; wax is the acid fast material. The acetone-soluble fraction, being a mixture of fatty a id calls forth varied responses. Tuberculoprotein is provocative of plasma cell infiltration. Th polysaccharides are chemotactic and toxic to neutrophile leucocytes and produce necrosis and hemorrhage.

*Lipogranuloma (Fat Necrosis) is characteri tically due to trauma with resultant* necrosis of underlying adipose tissue and the formation of a benign inflammatory

tumor The lesions are generally of hazelnut to walnut size and somewhat raised above the skin level. They are purplish or reddish at first firm but becoming cystic. The breast is a common location, and the tumor must be distinguished from malignancy (Dunphy: ASurg 38: 1 1939; Livingston and Lederer SGO 68: 230, 1939) The scrotum was the site in 3 fat little boys noted by Hinman and Johnson (JUrol 41: 726 1939) Trauma, accidental or surgical is the most frequent causative factor but a history of trauma was present in only 41 of 110 breast cases reviewed by Adair and Munzer (AmJSurg 74 117 1947) Attachment to the skin existed in many of these and the resemblance clinically to cancer was notable in 45 per cent positive diagnosis requires gross and microscopic examination of excised tissue.

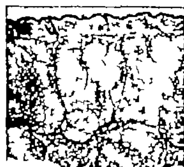


Fig 112.

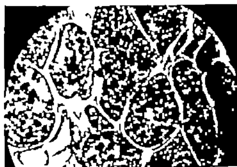


Fig 113.

Fig. 112.—Sclerema neonatorum. (Dr A. M. H. Gray.)

Fig. 113.—Sclerema neonatorum. Sudan III stain, showing disintegration, liquid fat, and cellular infiltration of fat globules (Dr A. M. H. Gray)

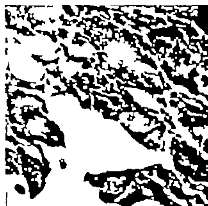


Fig 114

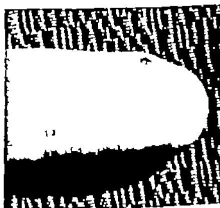


Fig. 115.

Fig 114.—Sclerema neonatorum. Subcutaneous tissue shows clefts indicative of fatty acid crystals, giant cell response to altered fat, and a rosette of crystals within giant cell in the upper right. (Patient of Dr Patricia Hart Drant. Courtesy Dr Frederick Weidman.)

Fig 115.—Asbestos corn (Alden and Howell ADS 49 312, 1944.)

The course of the lesion is chronic, with the likelihood of rupture through the skin and the discharge of sterile oily and caseous material. Histologic study reveals foreign body reaction with numerous phagocytes and giant cells. Treatment should be expectant in early cases, which may resorb. Excision, a speedy and satisfactory procedure, often becomes necessary

Refrigeration may produce adiponecrosis of the face with circumscribed, benign infiltration, which disappears spontaneously in a few weeks (Haxthausen: BJD 53: 83, 1941) Such cases have occurred in military aviation. See p. 70.

**Fat Necrosis in the Newborn (Sclerema)**.—Fat necrosis such as occurs in adults may also occur in infants. Gray (BJD 45: 493, 1933) distinguished (1) edema neonatorum, which is true edema, perhaps from hunger and hypoproteinemia (2) scleroderma, which is true scleroderma and very rare; (3) induration secondary to fatal disease, described as praegonia cadaveric induration of the celluloadipose tissue and (4) fat necrosis, or sclerema, which is a benign induration. This disease is a self limited, localized process affecting areas of the body often symmetrically situated

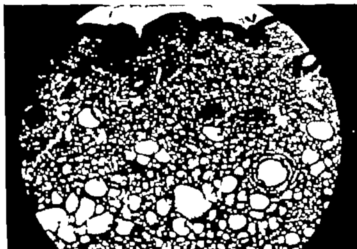


Fig. 116.—Paraffinoma, illustrating "Swiss cheese" structure.

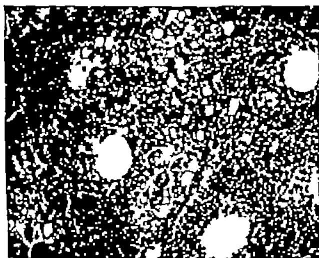


Fig. 117.—Phagocytosis of oil globules which have reached a lymph node in paraffinoma experimentally produced in a monkey (Dr Fred Weidman.)

over the bony prominences. The patients, born after difficult labor as a rule, are usually well nourished and of large size. The lesions become manifest in 2 to 20 days after birth as deep-seated, subcutaneous indurations. They range in size from small nodules to large areas covering the greater part of the back and buttocks, and appear to be slightly elevated above the skin. The color is usually bluish red at

the outset, suggesting at times a phlegmonous process. This disappears gradually the skin assuming its normal color even before the lesions have softened and disappeared. The surface of the skin is usually smooth. The lesions are not tender. The induration of the subcutaneous tissue does not pit on firm pressure nor does it allow the skin to be pinched up in folds. The hardness resembles that of wood or rubber. The areas have fairly well-defined borders, and small nodular lesions are usually freely movable. Fluctuation has occasionally been noted. The favorite sites are first the back, then the cheeks, arms, thighs, and buttocks. Almost every part of the body may be affected, except the palm and soles, abdomen inner aspect of the thighs, and axillae. An exceptional case with internal adipose tissue involvement was studied by Zeek and Madden (APath 41 166, 1946). The course of the disease includes a period of evolution and one of involution both processes may be present simultaneously. Softening and absorption of the indurated areas begin from the *fifth to the sixth week and are complete as a rule in 3 or 4 months. The lesions* disappear completely and only in rare instances do they leave any trace, such as slight atrophy. The general health usually remains good the temperature is not altered, and there is a steady normal increase in weight.

The pathologic process is essentially necrosi of fat cell and epithelioid and giant cell reaction. Protoplasmic meshes surround spaces formed by elongated needlelike crystals f neutral fat, which is dissol ed in preparation. In the fat cells there are similar crystals i rosettes or sheath. Some giant cells are filled with crystals radiating from the center. There is evidence (McIntosh et al. AmJDis Child 65 11 1933) that infant and adult fats are chemically different: in the newborn the melting poi t is higher tha normal body temperature because babies fat is lower in olei content than adult f t. Obstetrical trauma is the main precipitating factor in infantile fat necrosis, and the triglycerides are altered mainly in their physical aggregation, for in sclerodermatous tissues no lipase is present which *is demonstrably capable of hydrolyzing them.* Tuzzati and Ha sen (PSExpB 46 323, 1941) reported that the abnormal fat is largely palm tic an l in sclerema contains an excess of saturated fatty acids of low melting poi t and molecular weight.

**Paraffinoma (Oleogranuloma)** may follow i jectio of paraffin beneath the skin for cosmetic purposes. Such pseudo eoplasm develop in a fairly large percentage of the cases thu treated but a considerable period of time from 6 mo ths to 5 years, generally elapses before their appearance. The lesions are rounded or oval in outline and firm in consistency. I color they range from yellowish t reddish or purplish. Symptoms are practically absent but the deformity s sometimes extreme (Mook and Wander: AD8 1 304 1920 Gougerot BSocfrancD 41 1370, 1934). Simila lesio s develop following the inject on of paraffin mixtures employed as vehicles fo mercurials, campho and ther medicines (Brown et al. JLCM 29 ..39 1944; Conrad et al. J 121 237 1943). Injection treatment of hernia may cause them (Whittaker PSMMC 11 22 1936).

*In paraffinoma the foreign substance is encapsulated i fibroconnecti e tissue.* Cavernous spaces, surrounded by smaller ca ities, gi e the area a Swiss cheese appearance. The mass comprises granulati tissu like that of early tuberculosis before caseation. Oil droplets are encased in giant cells.

In diagnosis, one must distinguish fibroma, erythema induratum, and keloid. The location conformation, colo shape and history h uld suffice fo recognition.

The lesions progress to a certai poin and then remai stationary. It was once thought that the tumors were harmless but carcin ma and sarcoma ha e arisen in them. The only satisfactory treatment is total excision. X rays fail to benefit the condition as a rule.

**Oil Blast Gangrene.**—Fine droplets of unassimilable oil may be forced into the skin under high pressure i the operatio of D esel engines f a valve is opened during the operation of the machine and the body intercept th blast of oil droplets. Swelling, pain and, likely gangrene result. Prompt, free incision into the infiltrated *tissue may prevent sloughing (H ghes J 116 2849 1941).*

**Grease Gun Finger.**—An accident with a high pressure grease gun may f rce oil into the hand through a tiny pu ture. Surprisingly pai less t th time of the accident, swelling and numb ess bei g the immediate symptoms, pain follows, and gangrene is likely. The grease cannot be squeezed from the part even after incision (Byrne J 123 405 1944). Ai blast may cause comparable injury with emphysema (Desmond BMJ 1 442 194 ). Showers f spark may carry m ltiple metallic bodies int the tissues spot welding (B yoard and Smith BMJ 1 841, 1947).

Lycopodium may cause fore gn body gran loma. The spores, introduced by means of the surgeon's gloves into surgical wounds provoke inflammatory reaction

and masses of tubercle-like tissue at the site of the operation. Persistent sinuses as well as masses and adhesions may be the result. Such sinuses must be distinguished from tuberculous and actinomycotic lesions (Antopol and Robbins: J 100 1192, 1937)

**Trichome Dermatitis** is due to irritation by spicules, hairs, and scales of the epidermis of plants, particularly the cow itch tree of Australia (Laurence: MJAustral 1 16, 1933) Itchy papules on the extremities provoked by barberry thorns comprise another type of foreign body dermatitis (Schwartz ADS 37: 872, 1938) (Compare brown tail moth dermatitis and schistosome dermatitis.)

**Vaselinoderma** is follicular papular dermatitis due to foreign body reaction to petrolatum rubbed into the follicles of the skin (see Oil Acne p. 8?)

**Surgical Suture** material causing granuloma has interested many authors (Orr: ABurg 54: 87, 1947; Meade and Brewster: AmJSurg 45 419 1939) The lesions are small, sterile abscesses surrounded by dense fibrous tissue requiring sharp dissection for their removal.

**Silica and Silicates**, notoriously damaging to pulmonary tissues, also cause cutaneous lesions. Talc is magnesium silicate. Ground into the axillary skin by the pressure of a brace it caused a suppurative tumor in the case of deWaltsch (MAnnDC 9: 160 1940) Tissue reaction to subcutaneous injections of quartz were studied by Irwin and Gibson (CanadMAJ 39: 349 1939) Fiberglas spicules cause superficial irritation of handlers (Heinz J 124: 187, 1944) Talc on surgeons gloves may *provoke serious trouble (Lichtman et al.: SGO 83: 531, 1946) and gray nodules* of talc granuloma at edges of old scars were described by Flinberg (APath 24 36 1937) Potassium bitartrate (Seelig J 123: 113 1943) or heated gelatin powder (Correll and Wise: Sc 103 529 1947) may be substituted for talc on surgical gloves. Talc is an irritant ingredient of a powder intended for treating dermatitis of the feet if the epidermis is broken and silicate may meet mesoderm Asbestos spicules may provoke tiny warts on the fingers of those who handle it (Alden and Howell: ADS 49 312, 1944)

**Indelible Pencil Injuries.**—The basic aniline dyes used in making the leads of indelible pencils may provoke inflammatory necrotizing and foreign body reactions, the seriousness of which is partly dependent on their location Ocular injuries have frequently been reported, and in some cases the eye has been destroyed. The hands are especially liable to the injury The point of the pencil is accidentally introduced within the tissues and perhaps broken off The result depends on the chemical nature of the lead: toxicity increases among the aniline dyes from green yellow red, and brown to blue, methyl blue being sufficiently poisonous to cause systemic reactions such as diarrhea and icterus The acidic and neutral dyes cause little inflammation, but the basic ones do. Within an hour after the injury irritation is apparent, and within 24 hours there is evidence of necrosis, which is aseptic and lacking in leucocytes. The central semiliquid material is stained with the dye, and sloughing may continue or the necrotic matter may become walled off so as to form a pseudocyst, or perhaps it becomes merely a mass of colored granulation tissue. Since the dye dissolves slowly and diffuses slowly the lesions may persist for weeks or months, sometimes undergoing spontaneous acute inflammatory exacerbations. Best treatment, if it is anatomically applicable, is excision. To attempt to remove the fragile material with a forceps through a small hole results in crushing it and in the production of a violent exacerbation of the lesion. Mere incision and drainage is followed by recurrences of symptoms. (Mason and Allen AnnSurg 113 131 1941 hand cases; Sokolik AmJOphth 10 515 1927 eye cases.)

# DERMATOSES DUE TO VIRUSES

Viruses are probably organized bodies which are usually invisible by ordinary microscopic methods of examination. They have a diameter of less than 0.. μ and can often be filtered through candles and membranes impermeable to ordinary bacteria. They have not as yet been cultivated in cell-free media but they multiply freely in the presence of susceptible cells in vitro or in vivo. They frequently invade one particular species of host and tend to affect one particular tissue gi ing rise there to characteristic intracellular inclusion bodies, and they cause latent or overt infection followed as a rule by lasting immunity. The law of obligate communicability of virus infections was expounded, along with a able review of th nature of the agents by Rivers (BullNYAM 14: 383 1938). In the human being they produce diseases of as many varieties as bacteria do, with comparable properties of communicability. Since viruses do not live free, but must exist intracellularly, their ecology and epidemiology differ in important and characteristic ways from their bacterial analogues.

Viruses may be thought of as microorganisms, evolved by parasitic degeneration from larger organisms, manifesting reproductive acti ity, variation, survival, mutational and heritable faculties and interaction with their host (Burnet: Virus as Organism, Harvard U Press, 1945). Every virus particle like any other organism derives by genetic descent from some similar particle. Elementary bodies of *viruses are grouped within inclusion bodies which re intracellular* i *fowl pox,* accinia and m lluscum contagiosum, while the virus of herpes simplex invades and spreads in axis cylinders of peripheral nerves. Many human pathogens can be culti vated, and some cannot n the chick embryo (Goodpast re AnnIntM 13 1, 1939) See also Sanders APath 28 541 1939 (method of cultivation); Ebert and Otsuka: ADS 48 635, 1943 (review) Lem tte Sc 98 415, 1943 (size structure, chemistry); R vers Sc 85 10 1942 (immunology) Beveridge a d Burnet (Culti ation of Viruses and Rickettsiae n the Chick Embryo, HMSO London, 1946)

Exanthemas.—Under this title may be grouped the acute epidemic diseases with ki lesions which are important features of the diseases themselves, and which are of especial clinical importa ce in the recognit on of them. Several members of this group are f irus causation smallpox aricella measles, and German measles. Scarlet f r streptococcic.

## SMALLPOX

**Symptoms.**—The incubation period of variola varies from 8 to 12 days, and is usually about 10. The abrupt onset includes characteristically fever intense frontal headache severe lumbar backache, and vomiting. The eruption is first visible on the third or fourth day. It begins as a macular erythema, on which develop shotty papules in a few hours. These soon vesiculate, and they become pustular by the fifth day. There is *only one crop,* the lesions of which mature in the order of their appearance, earlier on the face and arms. The papules are usually discrete, but on the face confluence may occur and the extent of the eruption on the face is a measure of severity. The vesicles are tough, deep-set, multilocular and umbilicated. The pustules show less definite umbilication, and rest on a hyperemic base. They are smoothly rounded and of uniform size.

Usual Course.—Forehead and flexural surfaces of wrists are usually involved first. Face, forearms, palms, and soles seldom escape. Mucosae are generally involved. The abdomen is usually least affected, and the eruption on the trunk is discrete. The initial high fever falls with the appearance of the eruption, concomitantly with abatement of the con stitutional symptoms, but rises on the eighth or ninth day at the *maturity*



Fig. 118.—Smallpox, discrete eruption at its height (Dr S. D. Sweitzer.)



Fig. 119



Fig. 120.

Fig. 119.—Smallpox, 7th day of the eruption. (Dr J. F. Schamberg.)
Fig. 120.—Confluent smallpox.

of pustulation. On the ninth or tenth day of the eruption many pustules rupture spontaneously or as a result of slight trauma, and the lesions tend to desiccate, forming dry brownish crusts. Shedding generally extends over a period of a month or more. Scarring depends on the depth of the lesions and the extent to which destruction of connective tissue occurs. Secondary infection, as well as self inflicted trauma, abet damage done by the disease.

The virus survives for several months at least in the dry crusts (Downie and Dumbell, Lancet 1: 530, 1947).

**Varioloid** is smallpox which has been modified by previous vaccination and partial immunity. It is generally milder in every way. The lesions are fewer, smaller, and of briefer period of incubation, and there is less scarring.



Figs. 121 and 122.—Smallpox.



Fig. 123.—Confluent smallpox in an unvaccinated child.

**Alastrim (Variola Minor)** is milder than classic smallpox (variola major) but other diagnostic differences are not clear-cut.

**Diagnosis.**—In chicken pox, prodromal symptoms are brief and comparatively mild. The eruption comes early, is polymorphous, appears in successive crops for 3 to 5 days, matures rapidly and involves first the covered surfaces rather than exposed areas. Its vesicles are monolocular. They are superficial, fragile, and rarely umbilicated. Each rests on a wide, irregular erythematous flare. Cases of dermatitis medicamentosa, particularly from iodide and bromide, do not as a rule have severe constitutional symptoms, and the lesions do not involve the hands and wrists by predilection. History is important. In the pustular syphilid the papules are not hard or shotty. The varioliform syphilid prefers the perioral region especially in Negroes. There is no tendency to vesiculation. Constitutional symptoms are comparatively mild. There are general lymphadenitis, mucosal involvement, and positive serum reac-

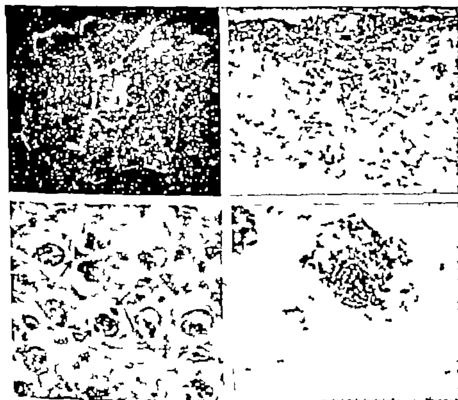


Fig. 121.—Cultivation and demonstration of virus of smallpox (Buddingh, G. J., Am. J. Hyg. 28: 130, 1938.)

*Upper left*, Chorioallantois of chick embryo, actual size, showing gross alteration produced by inoculation with variola 72 hours previously. The unfixed, fresh specimen; dark-field photograph.

*Upper right*, Chorioallantois, sectioned 72 hours after infection, showing inflammation of epithelium, proliferation, and vesicle formation.

*Lower left*, Guarnieri bodies, seen by high magnification of tissues shown at upper right.

*Lower right*, Paschen bodies seen in and about the smear of an infected epithelial cell; 72-hour lesion prepared by the Morosow technic.

tion. The usual diagnostic error made even by experts is to mistake smallpox for chicken pox (Smith BMJ 1 139 1948)

A flocculation test utilizing a suspension of material from the lesions incubated with an antivaccinal rabbit serum, is both rapid and useful (Craigie and Tulloch: Spec. Rpt. 156, M. Res. Council, London 1931)

Lesions of vaccinia and of variola can be distinguished in chick chorioallantois (North et al. MJAustral 1: 437 1944)

Scrapings from the bases of early lesions may be stained with Löffler's flagellar mordant and carbolfuchsin so as to demonstrate distinctive elementary bodies, larger than those of varicella (Van Rooyen and Illingworth: BMJ 326, 1944)



Fig. 125.—Vaccinia, accidental, on the hand.



Fig. 126.—Generalized vaccinia, the result of vaccinating a man who already had eczematous dermatitis. (Dr Fred Weidman.)

Paul's Test.—The content of the vesicopustules scraped with a sterile knife onto a glass slide and dried for 3 days, is taken up with 50 per cent glycerol in water and inoculated into the scarified cornea of a rabbit. Minute elevations of the corneal epithelium appear within 36 hours if the test is positive. Paschen bodies are found in these elevations.

Vaccination.—One applies a droplet of vaccine on the clean skin, which must be free of antiseptic (acetone may be used); the needle is pressed tangentially to the skin several times in such a manner that the point breaks the horny layer in area some 3 mm. across; and the lymph is allowed to dry. No dressing is necessary

COURSE OF NORMAL VACCINATION: On the first day there is a traumatic wheal. Nothing is visible for a day or so, then a tiny group of coalescing vesicles appears on a small zone of erythema. From the fifth to the ninth day the vesicle grows, and the area of redness extends. There is fever of 101 F to 102 F on the eighth and ninth days, with some malaise. The vesicle fluid is clear at first but becomes cloudy and eventually purulent. From the ninth to the twelfth day the zone of erythema spreads widely with thickening and induration of the surrounding skin after the twelfth day involution occurs with blackening, shrinking, and loosening of the crust at the periphery. The crust eventually drops off, leaving a red and pitted scar which slowly pales and becomes atrophic (The Jenner reaction, Gloyne: J 122 396, 1943)



Fig 127.—Milkers' warts. Lesions of first and second fingers of one patient, and of thumb of nother Severe lymphocytic inflammation and subepidermal vesicula tion are seen in the photomicrograph. (Bonnevie BJD 49 164, 1937)

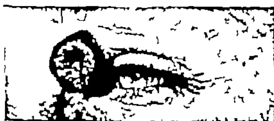


Fig. 128.—Orf The lesion, contracted from a sheep, here involves the eyelid. (Peterkin BJD 49 492, 1937)

INTRACUTANEOUS VACCINATION offers less opportunity for secondary infection, and by its use one *may secure a take in individuals who repeatedly fail to react to* ordinary methods. It may result in generalized vaccinia, or a nodular subcutaneous ses (Jacobs and Orris: *JPed 17 838, 1940.*)

COMPLICATIONS include regional or generalized (multiple) vaccinal lesions, urticaria, purpura, erythema multiforme and secondary infection such as infectious eczematoid dermatitis (Bloch Lancet 2: 504, 1919) rarely keloid (Skeer ADS 42: 1146, 1940) See Ourth et al. (JInvD 10: 197 1946)

REVACCINATION.—An individual who has been vaccinated will respond to subsequent vaccinations sometimes in the same degree as to the first. Usually how ever the lesion appears sooner and involutes more rapidly Revaccination is simple, harmless, and dependably protective. It hould be performed whenever real o suspected exposure to smallpox has been incurred.

GENERALIZED VACCINIA *is rare. It is likely howeve to compl cate the ill advised* vaccination of a person already suff ring from some widespread dermatitis.

Vaccinia complicating infantile eczema results in a typical syndrome resembling Kaposi's varicelliform eruption (Ellis J 104: 1801 1933). Death may result (Petermilgo and Toomey APed 61: 455, 1944). Clinical differentiation from Kaposi's eruption is possible (Riley and Callaway: J Invl) 9 321 1947).

**Milkers' Nodes.**—Nodular inflammatory lesions infectious and transmissible from cow to man and from man to man have been observed on the hands of milkers and others whose occupations bring them in contact with the usual source of the disease. It may give rise to epizootics in stock, especially in the summertime. Transmission to man may give rise to small epidemics. It produces characteristically granulomatous efflorescences at the sites of inoculation on the hands, with or without lymphangitis and secondary exanthemas. The disease disappears without treatment in a few weeks, leaving no trace. Histologic study reveals an infiltration of lymphocytes and fibroblasts with some polymorphonuclear leucocytes. There are no giant cells or plasma cells. The acanthotic epithelium shows some minute vesicles. There are no inclusion bodies, such as Guarnieri's. Paul's test is negative and patients take vaccinia in an ordinary fashion when inoculated (Becker J 115: 2140 1940).

**Orf (Sheep Pox).**—A contagious, pustular dermatitis of sheep known commonly as orf among veterinarians and farmers of Scotland, may be transmitted to man. In man Peterkin (BJD 49: 49* 1937) described the initial lesion as a dark red papule which grows to the diameter of a threepence or half-crown. It is firm and practically painless. It resembles a huge molluscum contagiosum tumor with well-marked central umbilication. The depressed center is covered with thin white skin and contains clear exudate. The exudate gradually becomes purulent, probably because of secondary infection and granulation soon heap up. If the lesions are treated with antiseptics, they tend to shrivel up in a few weeks without purulent discharge or granulation appearing. See Schoch (ADS 30 1040 1939), Nomland (ib 42 8 8 1940), Kingery and Dahl (ib 51 239 1945); Wallace (BJD 59 370 1947).

**Paravaccinia (Red Vaccinia).**—The lesion appears at the site of antismallpox vaccination as a red rounded, cruciform papule with precipitous margins. The pea-sized papule reaches its peak of development in 10 to 14 days and regresses gradually passing through the color changes of a hemorrhage.

**Diagnosis.**—The diseases of this group closely resemble one another. Peterkin distinguished orf from milkers' nodes by the fact that the lesion of orf in man is usually single, much larger than the lesion of milkers' nodes, is notably umbilicated, does not cause lymphangitis such as is often seen in milkers' nodes, and always heals by passing through a stage of resemblance to granuloma pyogenicum. Foreign body lesions due to hairs embedded in the skin of a milker's fingers are differentiated, such lesions being called *milker's panaritium*. Symmetrical calluses on the thumbs from milking in the Swiss method are plainly distinct from milkers' nodes.

## CHICKEN POX

**Symptoms.**—The period of incubation of varicella ranges from 11 to 24 days, averaging about 17. Droplet infection is the method of spread, and the disease is readily communicable. Infectiousness is slight after the sixth day of the rash (Gordon and Meader JAMA 93 2013 1929). The stage of invasion may be marked by some pyrexia, headache and malaise, but these symptoms are often altogether lacking. Lesions usually appear in crops. Trunk, face and scalp are the sites of predilection. Volar lesions are only occasionally present. The eruption is at first macular and erythematous, and vesicles and vesicopapules develop in the centers of these areas within a few hours. The vesicular lesions are pinhead to pea size, rounded, dome-shaped monolocular and translucent with or without pinkish red, hyperemic areolae. The vesicles rupture easily. If not broken by scratching they generally begin to desiccate at the end of 48 hours. There is some itching. The crusts are thin and of the same outline as the lesions. They become detached within a week to 10 days. The resultant scars are circular and atrophic.



Fig. 129



Fig. 130

Fig 129.—Chicken pox. (Dr J F Schamberg)
Fig. 130.—Chicken pox (Dr D Wood Ruggles)



Fig. 131.—Chicken pox vesicle, showing location of fluid in the epidermis which is free from inflammatory cellular infiltration. Endothelial destruction has allowed perivascular hemorrhage. Intense inflammation surrounds this vessel. (Johnson: Arch Path [illegible], 1940.)

Corneal involvement is probably not rare, and it apparently is not dangerous (Loewenstein BJOphth 24 391, 1940) It begins deep in the cornea and rises to the surface but does not induce photophobia. *Mucosal and visceral lesions have been described (Johnson: APath 30 292, 1940)* Intrauterine infection has occurred (Oppenheimer BullJHH 74 240 1944)

**Diagnosis**.—See Smallpox. The Paul test is negative in varicella. An eruption indistinguishable from varicella occurs in a small proportion of cases of herpes zoster particularly if severe (Bullowa AmJDisChild 49 923 927 1935) The relationship between the viruses of varicella and herpes zoster appears to be a close one but is debated. Postzoster serum may protect a varicella contact from developing the disease (Whigham *and Handelman BMJ 1 812, 1944)*

## MEASLES

**Symptoms**.—Rubeola is an acute, febrile virus infection characterized by catarrhal involvement of the upper respiratory tract and a diffuse erythematous, macular eruption which ends with fading and desquamation. The incubation period is fairly uniformly 8 to 10 days, but the appearance of the rash may rarely be delayed even until the twelfth day The onset of the disease is gradual, and *the early symptoms include slight fever* headache, chilliness, coryza, lachrymation, sneezing cough and photophobia. Lesions may be noted first on the buccal mucosa as small irregular bright red Koplik's spots each of which is marked centrally by a minute, bluish white speck. The eruption, which consists of small pinkish, slightly *edematous maculopapules, appears first on the face and neck and then* spreads rapidly to the trunk and extremities. On the abdomen and back, the lesions often tend to form crescentic or arcuate patches surrounded by normal skin. The eruption is of a deeper darker red than that occurring in scarlet fever The peculiar shotty lesions of variola are never present. The fever and the catarrh persist until the eruption begins to regress. *In* severe cases, hemorrhagic measles may develop with petechiae or even extravasations of blood into the lesions. After the eruption has persisted for 4 or 5 days, it gradually disappears, to be slowly followed by furfuraceous, branny desquamation.

## GERMAN MEASLES

**Symptoms**.—The period of incubation of rubella is probably between 14 and 21 days. *The onset is fairly abrupt,* and is characterized by mild constitutional symptoms and usually the enlargement of postauricular, suboccipital and postcervical lymph nodes. The eruption consists of rounded or oval, pinhead to split pea size pinkish macules or maculopapules. It usually appears first on the face, but quickly spreads to the chest, *trunk and limbs. The lesions are discrete as a rule,* but they may be grouped or even confluent. The rash seldom persists longer than 3 or 4 days, and its appearance is not followed by desquamation. Catarrhal symptoms, if present, are relatively mild. The patient's temperature seldom exceeds 100 F and there may be no fever whatever Relapses are infrequent. *While practically without complications to the patient,* rubella in pregnancy is highly hazardous to the fetus, especially during

the first 8 weeks, resulting in cataract, cardiac abnormality deaf mutism, and other anomalies (Albaugh J 129 719 1945)

**Diagnosis.**—German measles differs from scarlatina in these respects its longer period of incubation absence of severe systemic symptoms, particularly fever and angina first appearance of lesions on face and forehead and absence of desquamation. The pinkish, evanescent character of the lesions, relatively mild nature or absence of respiratory symptoms, and the presence of cervical lymph node enlargement will usually serve to distinguish it from measles.



Fig. 111—Morbilliform rash of German measles. (Dr J. F. Schamberg)

## HERPES SIMPLEX

**Symptoms.**—Herpes simplex is a virus infection commonly manifested as fever blisters, which comprise an acute eruption of a group of vesicles set on an erythematous, swollen base Early manifestations are sensations of itching and tension, followed by localized hyperemia. The patches are usually few in number and closely grouped Vesicles, which range from pin point to large pinhead size and which are filled with clear fluid, develop on the swollen reddened areas within a few hours. Suppuration may occur If unmolested, the vesicles dry up and form thin, yellowish or brownish crusts which drop off within 7 to 14 days. As a rule no scar results, but atrophic scars may follow severe cases. When the face is affected, the lips, perioral regions, and cheeks are the parts most frequently involved, although the external ear particularly the auricle, is occasionally attacked. The inner surfaces of the lips are sometimes affected. Herpes of the genitalia is frequent. Here abrasion is probable, and, when the patient is seen, only a group of raw circumscribed erosions, the bases of the former lesions, are visible The eruption can appear on any part of the body

Herpes simplex may be primary or secondary As a primary affection, its severity is occasionally considerable, with malaise, fever and satellite lymphadenitis. The constitutional symptoms of herpetic fever may precede the eruption some 24 hours or more. Secondary herpes occurs in the course of many febrile diseases, including the common cold, influenza, pneumonia, malaria, meningitis, and salmonella food poisoning It frequently follows sunburn or fever therapy and may be quite severe. Corneal involvement provokes acute disease with pain, lacrimation and photophobia,



Fig. 133.



Fig. 134.

Fig. 133.—Herpes simplex, with herpetic fever and painful lymphadenitis.

Fig. 134.—Herpes simplex. This patient's husband had a similar lesion, at the same time, on the left side of his chin.



Fig. 135.—Herpes simplex of penis.



Fig. 136.

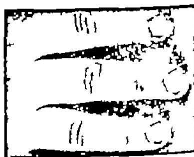


Fig. 137

Fig. 136.—Herpetic stomatitis.

Fig. 137.—Recurrent herpes in unusual location.

the epithelial lesion being characterized by swelling vacuolization and necrosis, multiple, dendritic or latticelike (Noé IowaSMSJ 29 400 1939) Cranial nerve palsies following general anesthetics were accompanied, for the most part by labial herpes and were attributed to herpes by Humphrey and McClelland (BMJ 1 315 1944) Herpetic encephalitis, with disorientation, drowsiness, scanty physical signs but severe histologic changes of malacia, has been recognized the 2 cases of Whitman et al. (J 131 1408 1946) were fatal.

Recurrent herpes probably is due to exacerbations of chronic herpetic infection. The lesions appear repeatedly at intervals of weeks or months in the same nerve region but not necessarily in identically the same spot. They may recur with the menses.

**Vesicular (Herpetic) Stomatitis.**—Dodd et al. (JPed 12: 95, 1938) reported 88 cases in children of a disease which was contagious and clinically identical with aphthous stomatitis.

The onset was sudden, with fever and malaise Within 24 hours lesions appeared on the tongue, the inner surfaces of the lips and th buccal and sublingual mucosa with swelling of the gums pain on eating, and cervical lymphadenitis. Herpes of the lip was present in 5 cases, and on the finger, perhaps from autoinoculation, in .. The disease was self limited. Familial infections occurred. This form of stomatitis was apparently identical with that generally described as aphthous stomatitis.

Inoculations of the corneas of rabbits produced transferable purulent keratoconjunctivitis; rabbits which survived infection w re immune to further inoculations, and were immune to herpes simplex, too.

Treatment is only symptomatic The patients should be isolated.

**Stomatitis and Diarrhea of Infants.**—Diarrhea may be the serious manifestation of an epidemic of herpes virus infection. While stomatitis is usually present at the early stage, generally about the anterio tongue region, vesicles disappear within 24 hours, leaving a red and excoriated surface that heals only after a week o two, and stomatitis may be quit mild or even overlooked (Buddingh: SMJ 39: 382, 1946)

**Vulvovaginal Herpes** produces a typical clinical picture with superficial erosive lesions of the labia majores and minores, symmetric tender ulcers with grayish-yellow membranes. Painful for a week and similar t ulcus vulvae acutum, it heals without scar Cases proved due to the herpes virus were recorded by Slavin and Gavett (PSExpBiol 63: 343 1940) See p. 19

**Etiology**—The cause of herpes is a filtrable virus. Supplemental factors which may provoke eruption are indigestion, febrile and toxic states, exposure to sunlight, and fever therapy The virus travels along motor sensory or sympathetic nerve fibers. If the content of a herpetic vesicle is inoculated into the scarified cornea of a rabbit, there results keratitis which is transmissible and which travels by way of the nerves into the brain. Inoculation into the brain produces encephalitis. Immunity to further inoculation develops after recovery The virus may persist despite high titer of antibodies in the host, and carriers exist (*Burnet and Lush* *Lancet* 1 629, 1939) *Genital lesions* in the female are not rare, and the disease may be transmitted as a venereal infection (Sharlit ADS 42 933 1940) Neutralizing antibodies, demonstrable by their inhibitory effect on chick chorioallantoic inoculations, are constantly present at a high level in individuals infected with herpes, and a heated preparation of the virus when inoculated intradermally provokes a specific erythematous reaction, regularly correlated with the presence of circulating antibodies, according to Nagler (JImm 48 213 1944)

**Pathology**—The vesicles are tough walled deeply seated, and intraepithelial. Eosinophilic inclusion bodies can be found within the nuclei

of ballooned epithelial cells. Dense perivascular infiltration with small round cells underlies the vesicles and follows the vessels deep beneath the surface lesion. This inflammatory reaction seems to provide fertile soil for cancerous proliferation for neoplastic leucoplakia commonly invades at the site of labial herpes simplex.

**Diagnosis.**—In vesicular contact dermatitis, the vesicles are close set, rupture readily exude gummy serum are associated with intense itching and are distributed on the skin without regard to the innervation. In impetigo contagiosa vesicles are discrete and autoinoculable, develop serially and reach mucosae only by extension. Herpes genitalis may be confused with chancroid, and rarely with chancre. In chancroid, painful ulceration is always present and the lesions, while often multiple, are never grouped as in herpes. As a rule syphilitic chancre is deeply infiltrated lymph node involvement is almost invariable, and dark field investigation is likely to reveal the spirochetes. The satellite gland of herpes is larger and sorer than that of the chancre.

**Prognosis.**—An attack seldom outlasts one week. Recurrences are likely Herpetic encephalitis is a grave complication rarely met in herpes simplex.

**Treatment.**—All sources of irritation and focal infection should be removed in recurrent cases. Locally, aluminum acetate, 1 500 in water is comforting applied by means of a bit of cotton as a cold pack. Spirits of camphor alcohol alone or with 0.2 per cent zinc sulfate added, or cologne water with 2 per cent alum may be prescribed but camphor and strong mentholated ointments are in our opinion of little value if not irritant. Ammoniated mercurial ointment is harmful. X ray therapy is advocated by some 2 or 3 doses of 100 r may be given.

IMMUNIZATION.—Freund (DmedWchn 54 356 1928) found that *guinea pigs vaccinated against smallpox manifest increased resistance to* the herpes virus, and that 7 patients with herpes had no further recurrences after such vaccination Vaccination is now recognized as a means of preventing recurrences of herpes simplex We have obtained many satisfactory results with intracutaneous vaccination. Moccasin venom 0.2 c.c. of 1 3 000 dilution given subcutaneously each week, may work when vaccine fails (Fisher ADS 43 444 1941)

## KAPOSI'S VARICELLIFORM ERUPTION

The disease was described by Kaposi (1887) as a complication of infantile eczema. The eruption closely resembles that of smallpox, but new lesions may appear for several days. Sudden in onset its umbilicated erythematovesicular elements rapidly develop on the face and head especially and the neck sometimes on the elbows and wrists as well. The lesions become pustular desiccate, and resemble those of chicken pox. Some scarring is usual. Fever precedes the eruption by 24 hours and persists for 1 or 2 weeks, falling by lysis.

The disease has been thought identical with generalized vaccinia It is true that generalized vaccinia occurs in persons with widespread dermatitis and in infants with eczema and that generalized vaccinia cannot readily be distinguished from Kaposi s eruption But the virus of herpes has been demonstrated in several cases, and while pathogenic cocci may also be found, Kaposi s disease is distinguished from vaccinia and may be defined as a specific varioliform manifestation of herpes (Barton

and Brunsting PSBIMC 18 199 1943 Wenner AmJDisChild 67: 247 1944; Lane and Herold ADS 50 396 1944 Lynch ib 51 129, 1945 Lynch and Stevens ib 55 827 1947) Pepple et al. (SMJ 35 667 1942) quoted Kaposi s description in full. Dennie discussing the paper noted that the disease does not immunize the patient to vaccinia

There were 17 deaths among the 67 cases reviewed by Barton and Brunsting (ADS 50 99, 1944) who demonstrated herpes virus in one of their patients. Of the 67 cases, 53 had atopic dermatitis, and 51 were 3 years of age or younger The 4 cases of Ruchman et al. (ADS 56 846, 1947) again proved to be due to herpes virus, included 3 adults who had been successfully vaccinated against smallpox.

In treatment, penicillin may be recommended only if secondary infection occurs, along with such efforts as may be suitable in smallpox. Symptomatic therapy may include boric-acid compresses and appropriate sedation.

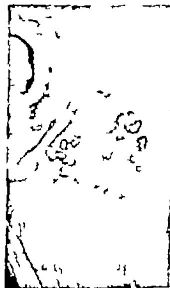


Fig. 116.—Kaposi' varicelliform eruption (Brown BJD 46 1, 1934)

## HERPES ZOSTER

**Symptoms.**—Herpes zoster (shingles) is an acute virus infection of nerve structures manifesting cutaneous lesions in the form of groups of vesicles distributed along one or more peripheral sensory nerves. The disease occurs perhaps more frequently in individuals who are overworked, ill, or affected by the absorption of certain drugs, particularly arsenic, but it has been observed even in the newborn (Freud et al. AmJDisChild 64 895 1942) The appearance of the eruption is generally preceded by malaise of variable severity and by neuralgic pain or hyperesthesia in the affected region. The lesions are vesicles seated on slightly elevated erythematous plaques. They appear in successive crops along the course of the affected nerve. The number of patches is 1 or 2 to 12 or more Each consists of half a dozen to a score of vesicles. In some cases, perhaps no visible lesions appear (see segmental neuralgia, p 463) In mild cases, only a few lesions develop the site of their location being hyperesthetic

for several hours before they are manifested. They persist for a week to a fortnight dry up form crusts, and disappear In severe cases, involvement may be intense and extensive. The vesicles range from pinhead to pea size and are usually filled with clear fluid Their walls are comparatively

Figs. 139 and 140.—Herpes zoster




Figs 141 and 142—Bilateral herpes zoster (Epstein ADS 34 [illegible] 1936)

tough. Their content may become seropurulent. Rarely the lesions are hemorrhagic. Gangrene may supervene due to either the severity of the disease or secondary necrotizing infection. In healing zona generally leaves corymbose atrophic white scars

Any neural segment may be involved. Lymph node enlargement is usual. It is regional. Pain is a variable symptom. In sturdy young persons the affection may give rise to little discomfort but in elderly persons pain is generally a prominent feature throughout the attack, and neuritic sequelae are common (Hamilton Pract 159 122 1947). The distribution of the eruption is practically always unilateral, although bilateral cases have been reported. Occasionally the disease may involve widely separated regions at one time. It is common to find scattered varicelloid lesions over the trunk during the eruptive period (Grindon, Jr ADS 39 865 1939)



Fig. 141.—Herpes zoster right eighth dorsal segment, 4th day of eruption (Dr B. N Andrade)



Fig. 144.—Herpes zoster early stage of eruption.

Involvement of the auricle may be associated with facial palsy or Ménière's complex (Wakeley and Mulvany Lancet 1 746 1939). *Hunt's syndrome* (aural herpes) is not necessarily due to geniculate ganglion disease, for cervical or other cranial nerve affection may cause otalgia, aural

herpes, and facial palsy (O'Neill AOtol 42 309 1945) Motor complications of zoster are neither rare nor remarkable, and weakness of an upper extremity in cases of branchial plexus zoster may persist for many months (Taterka and O'Sullivan J 122 737 1943) Unusual cases exemplifying motor involvement were noted by Parkinson (BMJ 1 8, 1948)

When zoster occurs in a patient with leukemia, especially lymphatic leukemia, nodules of leukemia cutis may appear in the herpetic dermatitis (Wile and Holman ADS 42 587 1940)

**Etiology and Pathology.**—A virus as the causative agent is strongly suspected but Fine (Filterable Virus Diseases in Man, Wood, 1932) stated that, while transmission to man has frequently been effected transmission to animals has been uncertain and filtrability has not been proved. Kundratiz (ZtschrfKinderh 39 379, 1925) transmitted zoster to 14 of 22 children inoculated with vesicle fluid. Arsenic may act either as an exciting or supplemental factor Small epidemics are common.

The vesicles are deeply seated, multilocular and involve the lower rete and papillary layer The cavities are filled with serum, disorganized prickle cells, and leucocytes. Some degenerated epithelial cells resemble protozoa and have been mistaken for parasites.

In the nervous system, histologic changes characteristic of zoster were found by Denny Brown et al. (ANeurP 51: 216, 1944): (1) ganglionitis showing necrosis and intense lymphocytic infiltration, with or without hemorrhage (2) poliomyelitis which is unilateral, localized, and segmental, and involves posterior horn and root; (3) mild localized leptomeningitis and (4) peripheral mononeuritis not only in the nerve distal to the ganglion but also in the anterior nerve root proximal and contiguous to the affected spinal ganglion. Spinal fluid changes, motor neuron involvement, and encephalomyelitis, with their resultant symptoms, were discussed by Gale and Abrahamson (AmJMSc 197 817 1939)

**Herpes Zoster and Varicella.**—The relationship between chickenpox and herpes zoster has received considerable attention. Some observers hold that herpes zoster actually is an atypical manifestation of chickenpox virus. Traub and Tolmach (NYSJM 31 107 1931) believed that evidence does not suffice to prove that the association is not fortuitous. Zoster is not transmitted as is herpes simplex to the rabbit's skin or cornea, and varicella does not immunize against zona, although the inoculation of zoster fluid into infants does indeed sometimes result in varicelliform eruptions (Brunsgaard: BJD 44 1 1932) Chorioallantoic inoculation experiments of Goodpasteur et al. (Edit. J 126 898, 1944) indicate that the viruses are not identical. See reports of Lynch (ADS 44 63, 1941) and Blatt et al. (JLCM 25: 951, 1940)

**Diagnosis.**—The neuritic distribution, pain, and course of the eruption are distinctive.

**Prognosis.**—One attack usually confers immunity The disease runs an acute course, and the eruption heals in from 14 to 30 days Hemorrhagic and gangrenous cases are serious. In supraorbital herpes zoster corneal damage sometimes occurs blindness may follow Scarring is variable Neuralgic sequelae are likely to last several months.

**Treatment.**—The administration of Phenacetin, amidopyrine aspirin, or sodium salicylate sometimes gives symptomatic relief. Occasionally resort must be had to morphine. Pain generally precludes the patient's continuance with his work he is better off at rest. Locally the use of counterirritation, such as ethyl chloride spray over the affected ganglion has been recommended. X ray therapy 200 r daily at 200 KV with 1 mm. Cu filtration over the affected root ganglia for 4 or 5 days, is helpful, best if started early (McCombs et al. AmJMSc 200 803, 1940) Thiamin in 2 000 unit doses yielded only indifferent results in the experi-

ence of Rattner and Roll (J 112 2585 1939) Intense ultraviolet erythema induced over the whole affected area stops pain, A.R Taylor told us. Comforting is a dusting powder freely applied and covered with a snug bandage. Melted paraffin may be applied as in the treatment of burns. Lesions may be incised and painted with gentian violet. Medical diathermy proves serviceable at times. Radiant heat is comforting Pituitary extract given by injection occasionally relieves the pain in a dramatic fashion (see J 115 2300 1940) The contraindications are coronary or myocardial disease hypertension, and pregnancy *Injection of 0.5 c.c. of 0 06 per cent* quinine and urea hydrochloride solution into the nerve so as to block it for a week gives prompt relief Lepp tells us, but Craig (PSMMC 11 677 1936) stated that even sectioning of the nerve may not relieve the pain. Findley and Patzer (J 128 1217 1945) preferred procaine infiltration of the appropriate sympathetic ganglion, and described in detail the technic of paravertebral block. Sulfonamides and penicillin are not useful here. Sodium iodide, 1 0 gm. intravenously each third or fourth day for 3 or 4 doses, is advocated by some practitioners.

## FOOT AND-MOUTH DISEASE

**Symptoms.**—Foot-and mouth disease is an epizootic infection of cattle, hogs, sheep, goats, and other animals, man being occasionally attacked. The virus is present in the fluid of th vesicles. Inoculation occurs through abrasions of the skin and mucous membranes. The disease was prevalent among the flocks and herds of England in the latter half f the nineteenth century, and many cases of stomatitis were attributed to it (Arkwright: Lancet 1 1191, 1928)

In man, the incubation period ranges from 2 to 5 or even 10 days. The onset of an attack is usually attended with constitutional symptoms of moderate severity and a feeling of dryness and burning in the mouth. The buccal mucosa becomes congested and swollen. W thin 2 or 3 days small vesicles develop on the lips, tongue and pharyngeal walls. *The manifestations of constitutional disturbance gradually subside.* After 48 to 72 hours the vesicles rupture spontaneously leaving reddish, extremely tender ulcers. The individual lesions are from 3 to 10 mm. in diameter They at first contain clear watery fluid but secondary pyogenic involvement is common. The regional lymph nodes are swollen and tender The ulcers usually heal promptly with little or no scarring (Sutton and O'Donnell J 66 947 1916)

**Etiology.**—Loeffler and Frosch (Zentralbl. f. Bakt. 23: 371, 1898) tried to free the vesicular lymph from corpuscular elements by passing it through Berkefeld filters; they *discovered that the filtrate was as actively provocative of the disease* i cattle as was unfiltered material. This was the first time animal disease had been shown to be d e to a filtrable virus. Pape and Waldmann (Berl. tierärz. Wchn. 3 : 249 449 1931) reported the successful transmission f the disease t guinea pigs by inoculation of the volar skin. Following this the animals become immune to that strain of the virus. This procedure is the customary diagnostic test; *it may not be performed in the United States without special permission from the Bureau f Animal Industry, permission which is not given excepting t State and Federal veterinarians.* See Waldmann (also YBD 1937 p. 196)

**Treatment.**—The course is self limited. Treatment is symptomatic if the disease exists, but the Waldmann vaccine prevents the disease in cattle (Rushmore BullUBAMD 3 94, 1945)

## WARTS

Warts are small, circumscribed, autoinoculable, epidermal and papillary growths. Several clinical forms are recognized.

**Verruca Vulgaris** is the common type. This kind begins as a tiny circumscribed, grayish, epidermal thickening The lesions are single or multiple, and become pinhead to pea size, rounded, papilliform excrescences. In color they are grayish, yellowish, or brownish. They give rise to no subjective symptoms. The lesions are usually discrete but may

coalesce, forming rugose plaques. Although the dorsal surfaces of the fingers, hands, and wrists are the sites of predilection, no region is exempt.

When the wart is shaved in the plane of the skin, radiating brown structures which are hypertrophied papillae become readily visible against the background of translucent callouslike epithelium. The hyperkeratotic material interstitially located between the papillae may be macerated or chewed away by a child and a digitate or filiform effect produced. Beneath the hyperkeratotic surface of a large wart, the epithelium is altered and becomes towlike and pasty. Using cautery or desiccation treatment one must wipe the corium bare of this.



Fig. 145.—Ordinary warts, with involvement of nail folds.



Fig. 146



Fig. 147

Fig. 146.—"Mosaic" plantar warts. (Montgomery and Montgomery: [illegible] 37: 1978, 1937.)
Fig. 147.—Verrucae planae juveniles.



Fig. 148



Fig. 149

Fig. 148.—Verruca vulgaris.
Fig. 149.—Filiform warts of the bearded region.



Fig. 150 Fig. 151 Fig. 152

Fig. 150.—Ordinary warts on fingers and hand (Dr Grover Wende)
Figs. 151 and 152.—Warts of paronychial skin.

Warts about the nails are often difficult to eradicate. The hyperkeratosis and elongation of papillae produced by the verrucous process are recognizable. The lesions involve the folds sometimes encircling the nail, occasionally pushing beneath it. Such lesions may be quite painful and of confusing clinical appearance. Picking at them and manicuring lead to their perionychial dissemination.

Warts of the eyelids may provoke conjunctivitis and keratitis as molluscum contagiosum does (deRötth: AOphth. 21: 409 1939)

**Verruca Plantaris.**—Lesions of peculiar aspect result when the palms and soles are involved. They are called "stone bruises" by the uninformed. This is a common condition, epidemics in schools being seen. The lesions are frequently located under the second metatarso-phalangeal joint or on the heel. They resemble small, oval calluses. They are sensitive, causing pain like a thorn in the foot. When the overlying epidermal "lid" is removed, a well like cavity partially filled with moist tough, tow colored corneous material is exposed, and tender bleeding tips of the hypertrophied papillae become apparent. They are carefully to be distinguished from calluses.



Fig. 153

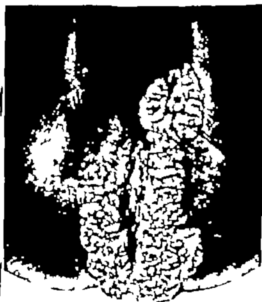


Fig. 154

Fig. 153.—Condyloma acuminatum. (Dr Sam Sweitzer's patient.)

Fig. 154.—Condyloma acuminatum of perianal and pudendal region in female. (Dr Oswald J Costa.)

**Mosaic Warts.**—Large composite patches of warts are seen fairly commonly on the sole. These are characteristically spread over a large area, are dry, comparatively painless, progressive and radioresistant. They are difficult to cure (the Montgomerys ADS 57 397 1948)

**Verrucae Planae.**—Flat warts are small polygonal yellowish or brownish, pinhead to pea size flat or dome topped growths which develop especially on the face, forehead and dorsal surfaces of the hands. They may be discrete but are usually grouped and may coalesce. They are

asymptomatic but are quite resistant to treatment. We believe that these are often disseminated by cold cream and hand lotions.

**Verruca Digitata.**—This variety which occurs most frequently on *the bearded region and scalp is characterized by its architectural* scheme, being composed of filiform projections with pointed horny caps, closely grouped on a narrow base

**Verruca Filiformis.**—This is a small, slender flexible, thread like growth, covered with smooth epidermis. The sites of predilection are the neck and the eyelids, and the bearded area in men, whose shaving inoculates and disseminates them widely



Fig. 184.—Histologic structure of ordinary wart showing extreme elongation of some dermal papillae, the tips of which, seen from above, give the appearance of "seeds." The normal epidermis at the base is sharply distinct from the noninflammatory dermis. The virus has provoked typical degeneration of more superficially located cells of the stratum germinativum.

**Verruca Acuminata.**—This variety, which is also known as condyloma acuminatum or venereal wart, develops near the mucocutaneous junctures in moist localities. The formations consist of closely aggregated collections of pointed, tufted or pedunculated pinkish or purplish projections of variable length and consistency In moist localities, such as about the vulva or beneath the foreskin, they become covered with pus, macerated epithelium, and decomposing secretions, and are offensive. They are autoinoculable *and seldom disappear spontaneously*

**Etiology**—Wile and Kingery (J 73 790 1919) inoculated warts successfully by intracutaneous injection of bacteria free filtrate of wart material. Templeton (ADS 32 102, 1935) obtained takes as long as a

Warts about the nails are often difficult to eradicate. The hyperkeratosis and elongation of papillae produced by the verrucous process are recognizable. The lesions involve the folds sometimes encircling the nail, occasionally pushing beneath it. Such lesions may be quite painful and of confusing clinical appearance. Picking at them and manicuring lead to their perionychial dissemination.

Warts of the eyelids may provoke conjunctivitis and keratitis as molluscum contagiosum does (deRötth: AOphth. 21: 409 1939)

**Verruca Plantaris.**—Lesions of peculiar aspect result when the palms and soles are involved They are called stone bruises by the uninformed. This is a common condition, epidemics in schools being seen. The lesions are frequently located under the second metatarso-phalangeal joint or on the heel They resemble small, oval calluses. They are sensitive, causing pain like a thorn in the foot. When the overlying epidermal lid is removed, a well like cavity partially filled with moist, tough, tow colored corneous material is exposed, and tender bleeding tips of the hypertrophied papillae become apparent. They are carefully to be distinguished from calluses.



Fig 153

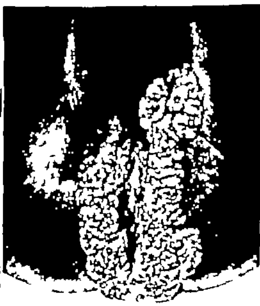


Fig 154

Fig 153.—Condyloma acuminatum. (Dr Sam Sweitzer' patient.)

Fig. 154.—Condyloma acuminatum of perineal and pudendal region in female (Dr Oswald J Costa)

**Mosaic Warts.**—Large composite patches of warts are seen fairly commonly on the sole. These are characteristically spread over a large area, are dry comparatively painless progressive and radioresistant They are difficult to cure (the Montgomerys ADS 57 397 1948)

**Verrucae Planae.**—Flat warts are small polygonal yellowish or brownish, pinhead to pea size flat or dome topped growths which develop especially on the face, forehead and dorsal surfaces of the hands. They may be discrete, but are usually grouped and may coalesce They are

VERRUCAE PLANAE.—A single, accurate careful application of Vleminckx's solution may suffice. The cautery can be used with suitable accuracy. Cannon (ADS 49 66 1944) recommended the ethyl chloride spray and curet, followed by 50 per cent phenol wiped off with alcohol.

PLANTAR WARTS.—Dependence is placed mainly on x rays or on radium. No filter is employed. The dose is best given with radium by surface application rather than by an x ray tube, the advantage being that with radium the intensity falls rapidly with distance from the source, and sharp reactions may be produced, as is necessary. Radon, 16 milli curie hours filtered with 0.3 mm. of steel, or 1,200 to 1,800 r single dose was recommended by Marks and Franseen (NEngJM 223 851 1940). If a single dose of 3 to 5 E through a portal not larger than 1 cm. does not cure, although it does in about 9 of 10 cases, some other attack should be undertaken. Electrodesiccation and electrocoagulation are preferred by many. Each wart should be treated individually. Surgery is not the first but the last resort in treating plantar warts, for they are likely to recur in the scar of an excision wound.

MOSAIC WARTS may respond to 60 per cent salicylic acid paste carefully delimited in its application, and occasional painting with strong silver nitrate solution (the Montgomerys ADS 45 1028, 1942). Thompson (BJD 55 267 1943) advised soaking the lesions for 10 minutes each evening in 3 per cent formol. The white macerated plugs that develop should be debrided and the treatment persisted with for the 3 to 8 weeks required for cure.

ACUMINATE WARTS AND CONDYLOMATA respond in a gratifying way to podophyllin. This resin, 25 per cent in liquid petrolatum, was reported efficient by Kaplan (NOrlMSJ 94 388 1942) a single application meticulously applied only to the moist warts being followed by considerable inflammation and then exfoliation. Culp and Kaplan (AnnSurg 120 251 1944) confirmed this observation, noting that, of 200 cases, 82 per cent were cured with one application and all were cured by a few subsequent applications. Cohen (Pract 156 133 1946) warned against transferring the agent to places where it is not desired. Sullivan found 20 per cent podophyllin in alcohol preferable and Marks (JMoMA 44 749 1947) recommended 15 per cent in compound tincture of benzoin for it stays where it is put. Podophyllin *must not* get into the eye, for it would cause severe and serious conjunctivitis. Its effect, Sullivan and King (ADS 56 30 1947) discovered, much resembles that of colchicine. Podophyllotoxin is the active ingredient of the resin (Sullivan et al. SMJ 41 336 1948).

## MOLLUSCUM CONTAGIOSUM

**Symptoms.**—Molluscum contagiosum ("water wart") is a virus disease of the epithelium characterized by small, waxy globular tumors which generally have minute rounded orifices at their apices. The lesions range in size from pin point to pinhead, and develop slowly. At first they are acuminate or globular in shape with broad bases, but as they grow larger they become flattened and umbilicated. The number of lesions is from 2 or 3 to 20 or more. The mucous surfaces, particularly the borders of the lips and lids, are occasionally involved. Lesions of the eyelids may provoke mild conjunctivitis. The lesions are at first firm but become somewhat softened and ultimately may suppurate, finally healing without scar. Sometimes the tumors disappear spontaneously but if un

treated generally persist for many months. The lesions are discrete and may be grouped. They give rise to no symptoms unless infected. Numerous and minute miliary mollusca resemble verrucae planae.

**Etiology and Pathology.**—A like disease occurs in birds, fowl pox, and in animals. It is autoinoculable and contagious. Juliusberg (D med Wchn 33 1698 1905) demonstrated the filtrable nature of the causative

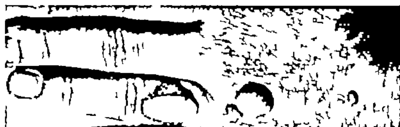
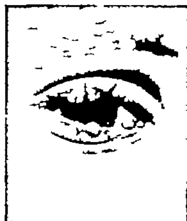


Fig. 156.—Molluscum contagiosum. (Dr Roochsee.)





Figs. 157 and 158.—Molluscum contagiosum.









Fig. 159.—Molluscum contagiosum, microdissection of infected epithelial cell (Van Rooyen, J Path Bact 46 425, 1938.) A One needle in cell to steady it, other in molluscum body. B Molluscum body moved slightly, both needles in focus. C Molluscum body taken from bed, which remains a cavity.

agent in human beings. *Strongyloplasma hominis* is manifest as spheric particles which are 0.25 micron in diameter numerous and nonmotile in fresh preparations. Aggregates of them form acidophilic inclusion bodies within the cytoplasm of infected epithelial cells. The lesions are formed by hyperplasia of infected epithelial cells. Cytoplasmic inclusions push aside the nuclei and bulge the cell walls (Merrowsky et al. JInvD 7 165 1946) Fragments of an inclusion body in fowl pox were proved to be infectious by Woodruff and Goodpasture (AmJP 6 713 1930) Intracerebral inoculation of the virus in chicks produced a characteristic and fatal disease (Buddingh JExpM 67 921, 933 1938) An attack of molluscum contagiosum does not confer immunity and while its virus and that of birdpox are similar the two diseases are quite different (Low EdinMJ 53 657 1946)

**Diagnosis.**—The size, color and appearance of the lesions, together with the fact that their contents can be squeezed out, are distinctive. Fibromas, milia, comedones, and verrucae are to be excluded.

**Prognosis and Treatment.**—The disorder is primarily harmless, but the lesions if untreated are persistent and if secondarily infected are painful and dangerous. On the eyelids, they may cause conjunctivitis One should incise, squeeze out the contents, and apply tincture of iodine to the cavities. Fulguration is effective (Goodman BJD 47 413 1935) Sulfadiazine in a dose of 4 gm. per day will cure in a week or two Laymon (ADS 53 643, 1946) reported in confirmation of Sommerville (BJD 53 255 1941) and this approach may be desirable when lesions are so numerous that surgical methods would be difficult Schiff (RhodeIMJ 30 806, 1947) succeeded in a miliary case with sulfadiazine but we have failed in * instances.

## LYMPHOGRANULOMA VENEREUM

**Symptoms.**—Venereal lymphogranuloma is an infectious disease which is generally transmitted by sexual activity The first symptom is often a small ulceration a papule or a herpeslike lesion of the genitals. The character of this primary lesion, which often is unrecognized, is variable Primary anorectal inoculation probably occurs (Grace and Henry NYSJM 40: 285 1940) The incubation period is thought to range from 2 to 6 weeks from inoculation to lymph node enlargement. The primary sore is often on the prepuce, but adenitis may precede the appearance of a recognized primary A genital lesion may start to heal when the bubo develops, but in the absence of bubo the ulcerations may be resistant (Brandt VDI 22 248, 1941) In women, the portal of entry may remain obscure. The nodes which drain the portal of entry usually the inguinal nodes of one or both sides, become swollen and tender and ultimately the overlying skin assumes a purplish hue and finally ulcerates Multiple sinuses connect the suppurating nodes with the surface Healing is slow and cicatrices are thick and puckered. Adenitis was bilateral in 21 per cent of the cases of Prehn (ADS 35 231 1937) and it showed no predilection as to side. Lymph nodes became suppurative in 75 per cent of the cases. The temperature averaged 100° F the highest noted was 106 F Slight anemia and slight mononucleosis characterized the blood picture. Contact infections are possible Cases have involved the tongue and submaxillary glands. Hellerstrom described infection of a physician s finger; the axillary lymphatics underwent the usual course of venereal

lymphogranuloma. Extragenital lesions, including those of head and neck, were reviewed by Slaughter (SGO 24 390 1940)

ANORECTAL LYMPHATICS rather than the inguinal may be involved, usually in women for anatomic reasons. The chronic inflammatory response and lymphatic obstruction lead to rectal stricture and perineal distortion even elephantiasis, esthiomene This becomes a most stubborn



Fig 160 —Venereal lymphogranuloma penile lesion and lymphadenopathy Note te positiv Frei test reactions on forearm. (Cole J 101 1949 1933)



Fig 161 —Anorectal syndrome with rectal stricture (Cole J 101 1949 1933)

and resistant condition The chronic ulcerative process involving the labia, perineum anus, and lower rectum may be of the superficial perforating hypertrophic or mixed type Rectal strictures involve the female by preference. The stricture is located in the lower 10 cm of the bowel, generally not higher than 6 cm It may be bandlike or tubular It has been seen in male homosexuals Treatment is indeed unsatisfactory Some

cases of ulcerative colitis are due to venereal lymphogranuloma. Urethral anorectal, and genital syndromes in women overlap

Constitutional Symptoms, Exanthems and Complications.—Along with local lymph node reaction, one occasionally finds a generalized lymph node enlargement. The spleen may be enlarged. Polyarthritis may be present. Abdominal and pelvic inflammation have been shown due to lymphogranulomatosis in fatal cases. General skin manifestations, such as erythema nodosum, erythema multiformelike eruptions, urticaria, scarlatiniform eruptions, and disseminated ulceration have been noted. A rash was elicited by exposure to sunshine in 60 per cent of women with chronic disease, a smaller proportion of acute cases and of cases in males, according to Sonck (abs ADS 54 216 1946) Erythematous papules and wheals were noted, sometimes quite itchy affecting especially the extensor aspects of the extremities. Photosensitivity apparently occurs from 5 to 6 weeks after the glandular symptoms start and it disappears when the disease is cured.

Ocular Lesions have been attributed to lymphogranuloma venereum (Macnie: AJOphth 25: 285 1941)

Parinaud's syndrome and keratoconjunctivitis have been proved to be of this nature (Scheie et al.: J 133: 322, 1947)

Genitourinary Manifestations may be primary with infection of meatus or urethritis. Later stricture of the urethra or perigenital sinuses and fistulae may develop. Invasion of the posterior urethra and spread to prostate seminal vesicles, and epididymis may take place. Secondarily the bladder neck may be deformed, displaced, or compressed, and even the pelvic ureter may be forced to dilate (Coutts JUrol 49 545, 1943.) Urethral discharge with inguinal adenopathy calls for a Frei test for the primary sore of lymphopathia may be intraurethral just as the syphilitic chancre may be.

Pregnancy and lymphogranuloma venereum rarely influence one another unless mechanical interference occurs (Wilson and Hesseltine AmJOG 43 439 1942)

Bone and Joint Manifestations are not common, but arthralgia, acute polyarthritis, and chronic recurrent polyarthritis have been noted In 2 of 4 such patients of Hickam (ADS 51: 330, 1945) pustular eruption and fever followed Frei testing Osseous lesions were reviewed by Wright and Logan (AмSurg 39 108 1939) they described instances of necrosis of the pubes possibly due to direct extension of the infection.

Neurologic Involvement was described by v Haam and D Asmoy (J 106 104 1936) whose patients had fever headache, vomiting, and painful stiffness of the neck. Active virus was obtained from the spinal fluid. The spinal fluid showed enormous increase of total protein but responded to sulfonamide therapy in the cases of acute meningoencephalitis of Zarafonetis (KPracJM 39 367 1944) Ocular involvement was reviewed by Espildora and Coutts (AmJOphth 25 916, 1942)

**Etiology Pathology and Diagnosis.**—The presence of venereal lymphogranuloma infection is often obfuscated by other venereal diseases. No special racial susceptibility is discerned although Negroes are often the victims.

In studying the venereal transmission of the disease and the high preponderance of male victims, Bejarano and Calatayud (Crom. Méd. 1933, p. 721) found 11 per cent of 73 apparently healthy prostitutes gave strongly positive Frei test despite negative histories and examinations. Some observers believe that a woman may be a carrier of the disease without being a sufferer from it

The inflammatory process may be acute, subacute or chronic, according to Kornblith (SGO 63: 96, 1936) who determined that the histologic unit of the disease is an inflammatory nodule which undergoes necrosis

The Virus.—Hellerstrom demonstrated the existence of a filtrable virus as the cause and he transmitted the infection to animals. Miyagawa (JapJD 39 103, 1936) reported the cultivation of the virus in the allantois of chick embryos. Wilmoth (JTropM 39 172, 1936) accomplished transmission of the disease to human beings

by means of virus grown artificially. Beautiful illustrations of virus colonies developing in the epithelial cells of corneal cultures from puppy embryos were published by Malamos (ZfBakt 143: 1, 1938).

FREI TEST.—Frei (J 110: 1633, 1938) first demonstrated a specific skin reaction with sterile bubo pus. The reaction becomes positive within a few weeks after the adenitis appears. The Frei test reactivity apparently remains positive during life, once it has become positive. It is uniformly positive if the bubo has lasted 40 days. Mouse brain or chick yolk sac infections provide satisfactory antigens.

The Frei test is a small-scale reproduction of the disease. The typical nodule comprises a shell of palisaded layers of epithelioid cells with a central granular core composed of the debris of leucocytes, lymphocytes, and endothelial cells. Plasma cells develop after the more acute phase. The spread of the process may lead to the formation of sinuses or abscesses; the involved glands may coalesce or remain distinct. Sometimes there occurs spontaneous healing. Donovan bodies are not found in lymphogranuloma inguinale and lymphogranuloma inguinale is refractory to treatment with tartar emetic, a remedy which has proved of great value in combating granuloma inguinale.



Fig. 162.



Fig. 163.

Fig. 162.—Lymphopathia venereum. (Dr. O. G. Costa.)

Fig. 163.—Venereal lymphogranuloma. Epithelioid nodule in lymph node. Note leucocytes and plasma cells in center and presence of extensive necrosis. (Korabiter, ZfO 61: 89, 1936.)

COMPLEMENT FIXATION TESTS probably have significance (Beeson and Miller: AmJPubH 34: 1076, 1944).

SERUM PROTEINS are increased by the infection, sometimes before the Frei test becomes positive. Serum protein exceeded 8 gm./100 c.c. in 63 of 67 cases of Kampmeier et al. (AmJMSc 198: 516, 1939). While this change is not specifically diagnostic, it is significant, and hyperglobulinemia responds to sulfonamide treatment (Schamberg: AmJMSc 201: 67, 1941). The formol gel test, indicative of hyperglobulinemia, affords reliable help in diagnosis and interpretation of response of the disease to treatment, according to Combes et al. (AmJS 29: 611, 1945).

**Treatment.**—Surgical removal of infected lymph nodes was at one time recommended, but injections of Frei antigen and the use of sulfonamides are followed by better results. Fluctuant buboes should be

aspirated (Kornblith AmJDigD 6 712, 1939) Best vaccine treatment is by alternate, continuous courses of subcutaneous or intravenous injections of specific antigen, with a short rest period following the end of each intravenous course. Focal reactions and variable febrile and constitutional symptoms may be expected. Supportive measures should be maintained during courses of injections and rest periods. These include the urging of fluids, bed rest, and light diet during the febrile stage of the disease aspirin medication and local heat applications for arthralgia and myalgia aspiration of fluctuant buboes, enemas daily of 1:5 000 potassium permanganate, low residue diet, mineral oil and mild laxatives for anorectal cases iron medication for secondary anemia douches and the frequent application of 25 per cent balsam of Peru ointment for vulvar and vaginal ulceration. Colostomy is likely to become necessary in rectal cases. Potassium antimony tartrate, 5 c.c. of the 1 per cent solution given twice a week, may be beneficial in the early stages. Lithium antimony thiomalate (Anthiomaline) was recommended by Law (Lancet 1 300 1943) Mice infected experimentally can be saved by sulfanilamide, a therapeutic response different from that of other virus diseases, excepting influenza (MacCallum and Findlay Lancet 2 136 1938) Sulfanilamide has been used in human cases with good effect (Shaffer and Arnold ADS 38 705 1938) The dose must be large Probably the best treatment at present available comprises Frei vaccine intravenously on alternate days, sulfanilamide rest and artificial fever therapy in hospital (Costello and Cohen ADS 44 391, 1941) Autogenous blood serum contains specific antigen and may be injected subcutaneously in treatment (Marks SMJ 35 1092, 1942) Injection of the specific antigen may provoke undesirably severe systemic reactions and rashes. After review of 388 cases at Bellevue Hospital Costello and D Avanzo (ADS 57 112, 1948) concluded that sulfonamides and bed rest comprise the best treatment in the early stage

Aureomycin, an antibiotic derived from a Streptomyces (see p. 42) has exhibited striking activity against many rickettsiae and certain viruses, and is highly effective in the treatment of mice infected intracerebrally with the virus of lymphogranuloma venereum Available to Wright et al. (J 138 408 1948) in vials containing 20 mg (Lederle) to be dissolved in 2 c.c. of saline and injected intramuscularly it was given to human cases in doses of from 10 to 40 mg per day In all cases so treated there was reduction of the size of buboes within 4 days, and the inclusion and elementary bodies showed degeneration and disappearance within 48 hours.

# DERMATOSES DUE TO RICKETTSIAE

Rickettsiae, like viruses, are obligate intracellular parasites. They are, for the most part, microscopically visible gram negative bacteria like bodies found in the alimentary canals of arthropods and frequently associated with disease in man and animals.

The diseases of man with which species of Rickettsia are associated and of which the epidemiologic character is determined by the life cycles and the feeding habits of the arthropod vectors may be divided into four subdivisions: typhus, Rocky Mountain spotted fever, tsutsugamushi, and Q fever, according to Dyer (J 124: 1165, 1944) whose résumé we quote here extensively. The organisms of Q fever, which is not associated with dermatologic symptoms, pass bacterial filters which retain other pathogenic rickettsiae.

A characteristic of this group of diseases with the exception of Q fever is the production in patients of agglutinins for the X strains of *B proteus*. Serums from typhus and spotted fever agglutinate the $OX_{19}$ and $OX_2$ strains, while those from tsutsugamushi agglutinate the OXK strain, typically but no strain of *B proteus* has been found which is agglutinated by serums from Q fever. The absence of cross immunity also separates subdivisions of rickettsial infections.

Clinically the typhus, spotted fever and tsutsugamushi groups are characterized by sudden onset, rash, fever of fairly well-defined duration, mental disturbance and pronounced prostration. Epidemic (louse-borne) and endemic (murine or flea borne) types of the typhus subdivision are recognized. The Rocky Mountain spotted fever subdivision is not so clearly delineated but includes other or similar tick-borne diseases, such as boutonneuse fever, the misnamed São Paulo exanthematic typhus, the so called tick typhus of India, and South African tick bite fever. The tsutsugamushi subdivision embraces also scrub typhus and other mite borne diseases of southern Asia and the Southwest Pacific islands.

Pathologically characteristic changes consisting of vasculitis and perivasculitis are caused by rickettsiae which, if carefully sought, can usually be found in the endothelial cells lining the blood vessels especially the smaller ones of the brain, lungs, heart, and skin (Mandelbaum and Hollander AmJ 3 315, 1947). A skin biopsy, selecting a well-developed lesion of the macula type, is excised sharp, fixed in Regaud's fluid and stained by the Giemsa method. Rickettsiae can usually be found, but if they are not the proliferative endangiitis is diagnostic.

**Epidemic Typhus.**—The body louse and the head louse, which are probably not different species, carry typhus (*R prowazeki*) from one human being to another. The infection kills the louse within 12 days (Parker J 110 1185 1293 1938). The incubation period is from 5 to 15 days, usually 8 to 12 days. Onset may be preceded by a day or two of malaise but the majority of cases show abrupt onset with rapidly rising fever, repeated but seldom severe chills, and headache. Fever rises steadily, reaching a maximum by the end of the first week, with slight morning recessions. Fever falls by rapid lysis after about 14 days. Headache is a prominent symptom hard to relieve. Prostration and cardiac weakness *may be evident from the start. In severe cases with cardiac weakness*, there is a tendency toward development of gangrene of the extremities. Confusion, disorientation, restlessness, irritability, even delirium occur.

The most characteristic feature of the disease is the rash, which appears about the fourth to sixth day, perhaps as early as the third day or as late as the ninth. Rose-red macules and papules, at first erythematous but later purpuric, increase in number and extend for perhaps 48 hours, their profusion being related to the severity of the disease. They occur

first on the inner surfaces of the upper arms or on the sides of the chest and upper abdomen, then spread to the rest of the chest, trunk, and extremities, even including palms and soles, but seldom affecting the neck and face. The rash becomes brownish as recovery ensues and eventually disappears. The fatality rate ranges from 20 to 80 per cent in different epidemics.

**Endemic Typhus**, differing from epidemic chiefly in epidemiology, is due to *R. mooseri*, and cases have occurred in every state of the United States. There is a reservoir of infection in the common rat and possibly in other rodents, transmission from rat to rat probably being accomplished by rat fleas and lice. Transmission to man probably is accomplished by infected feces of rat fleas. Clinical manifestations differ from those of epidemic typhus mainly in being milder. The rash seldom appears before the fifth day and may comprise only a few macules which soon disappear. Pink maculopapules becoming bluish red and slaty were described by Donald and Barker (BMJ 2: 333, 1942) appearing first on the shoulders, about the axillary folds, then the upper abdomen and flanks, later on trunk and limbs, and prominent on the forearms and dorsa of hands and feet. Fading is succeeded by mottling which may last for a month, with fine branny desquamation.

**Rocky Mountain Spotted Fever** is found chiefly in the northwestern states of the Union, prevalent in sheep-herding districts. The disease in man has occurred in most of the 48 states. It affects especially outdoor people in the spring and early summer in the West, later in summer in higher altitudes. In any locale the mortality rate is about constant. In the Bitterroot Valley region of Western Montana the rate in adults is about 80 per cent, 35 in infants. In the East it runs about 25 per cent.

The attack may be abortive, fulminating, or of any degree of severity in between. In ambulatory cases the fever is low, the rash scanty, and the duration only 14 days. A temperature of 104° F. with fleeting rash and recovery in a week, characterizes the abortive case. Fulminating infections kill in 3 to 5 days with or without a rash, which may be blotchy and ecchymotic. The incubation period of severe cases is 2 to 5 days and is prolonged to 3 to 14 days in milder cases. There may be a 2- or 3-day period of prodromal malaise, or the onset may be sudden. It is marked by chill, headache, pain in the upper abdomen, and pains in bones and muscles. The main complaints are frontal and occipital headache, low back pain, and malaise. The rash depends pathologically on endangiitis of peripheral vessels. It appears on the second, third, or fourth day, rarely a day or two later. It is first seen on the wrists and ankles, and spreads rapidly to the back, then to the arms, legs, and chest, and last to the abdomen. Palms and soles are frequently involved, often the face and occasionally even the scalp. First pale and simulating the early rash of measles, it becomes bright rose in color and maculopapular. The exanthem soon becomes purpuric and bluish. Large, sparsely distributed bright spots are of better prognostic import than small ones tending to become confluent. The rash comes in crops, of which there may be one, two, or three. Sloughs due to endothelial necrosis may involve the scrotum, prepuce, vulva, buttocks, or palate. The fever persists for 2 or 3 weeks, and the eruption clears as bruises do if the patient recovers. Desquamation occurs at the end of the third or fourth week (Hutton: J 117: 413, 1941).

Etiology.—*Dermacentor andersoni, D. variabilis* (dog tick) and *Haemaphysalis leporis-palustris* (rabbit tick) can carry *R. ricketts*-

which causes spotted fever and others have been proved capable of carrying it. The virus is not transmitted until the tick has been feeding for 8 to 24 hours. The patient of Bauersfeld (J 112: 1819 1939) was infected by removing a tick from her husband, and she died.

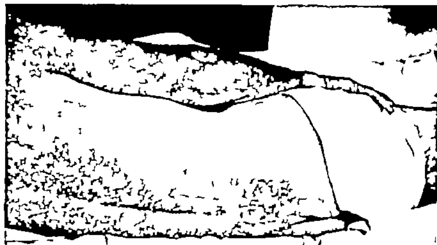


Fig. 164 —Rocky Mountain spotted fever (Dr J J Eppy)

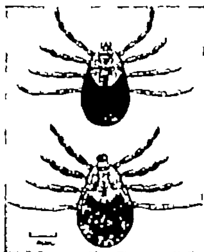


Fig. 165.

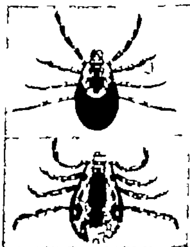


Fig. 166.

Fig. 165.—*Dermacentor andersoni*, female above, male below (Dr F C. Bishopp, U S. Dept. Agriculture, Bureau of Entomology and Plant Quarantine.)

Fig. 166.—*Dermacentor variabilis* female above, male below (Dr F C. Bishopp.)

TREATMENT —Rest, hospital care, and symptomatic and supportive treatment are required *in cases which are not mild*. *Neoarsphenamine* dissolved in aqueous Metaphen was recommended by Reich (AnnIntM 17: 247 1942) Topping's anti-spotted fever rabbit serum may be dramatic if given early in a dose of 1 c.c per kg., according to Meade (VaMMonth

73: 216, 1946) Para-aminobenzoic acid given in large doses is of real utility (Rose et al. J 129: 1160 1945 Flinn et al.: ib. 132 911 1946; Tierney SMJ 40 81, 1947 Ravenel ib 40 801, 1947) The dose is 6 to 8 gm. initially then 2 or 3 gm. each 3 hours. To be effective it is to be started before the end of the first week. The blood concentration should be kept around 30 to 40 mg per cent The WBC must be watched and the drug stopped if leucocytes number less than 3 000 Methylthionine chloride, 0.2 per cent, added to the diet of experimentally infected mice was more effective than PABA (McLimans and Grant Sc 105 181, 1947) Pointing to the loss of protein and low serum levels which develop Harrell et al. (SMJ 39 551 1946) urged a high protein diet, because the antiserum, admittedly valuable if given before the third day does not prevent protein depletion. Treatment of a comprehensive sort includes restoration of fluid and electrolyte balance by intravenous dextrose in saline or lactate-Ringer s solution, correction of acidosis by one-sixth molar sodium lactate correction of serum protein depletion by intravenous plasma, provision of high vitamin intake, administration of PABA with alertness to its possible intolerance, and attention to possible complications such as congestive heart *failure pneumonia, and thrombophlebitis (Ravenel: J 133 989 1947)*



Fig. 167



Fig. 168.

Fig. 167—Tick bite fever initial sore on cheek. (Dr A. Pijper)

Fig. 168.—Larva of *Rhipicephalus appendiculatus* the common vector of tick bite fever in South Africa. (Dr A Pijper)

CHLOROMYCETIN a crystalline product of the growth of a Streptomyces, inhibits various viruses, rickettsiae and bacteria, protecti g chick embryos and mice from infection (Ehrlich et al.: Sc 106 417 1947) Effective and nontoxic when given orally doses of 1.0 gm. initially followed by 0._ gm. each 4 hours cured typhus in human beings (Smadel et al.: cited J 138 432, 1948; BMJ 2 428, 1948) It is dramatically beneficial in scrub typhus, and it may be expected to revolutionize therapy of several diseases, especially the rickettsioses.

PROPHYLAXIS AND CONTROL.—One should wear boots, leggings, and puttees, and hunt for and remove ticks twice day the search must miss no area of the body All clothing should be removed at night. Persons hould sleep separately Th clothes must be kept off the ground. I choosing a camp site, elect timbe country and scant vegetation. Avoid rodents, sagebrush, and old trails. One should avoid infected areas. Dibutyl phthalate rubbed into the clothing gives protection and withstands several launderings f the garments (Connell Rpt. BMJ 3 787 1946)

VACCINE is prepared by grinding infected ticks to make a phenolized emulsion; after settling, the supernatant fluid is used. It is given in two subcutaneous injections of 3 c.c. each for adults and 1 c.c each for children under 10 years; 3 injections may be given instead of 2. Children are better protected than adults. The vaccination must be repeated annually in the spring and it will protect for the remainder of the year. See Cox (Sc 94: 399 1941); Parker (AmJTropM 21: 369 1941)

**Rat-Mite Dermatitis.**—Dove and Shelmire (J 97 1506, 1931) described an acariasis in northern Texas due to the blood-sucking rat mite, *Liponyssus bacoti Hirst*. These mites can convey endemic typhus, or Brill's disease. If they are infected, a febrile course follows their bites and persists for about two weeks.

**Tick Bite Fever.**—South African tick-bite fever is due to rickettsial infection. It closely resembles fièvre boutonneuse, kedani and tsutsugamushi. In the region of Lorenzo Marques, no newcomer escapes this mild disease, which is without mortality. In certain areas infected larval ticks, *Amblyomma hebraeum*, are numerous in the tall grass. Their bite results in a pathognomonic initial sore, a raised, bright red circular indurated lesion of 2 cm. diameter with a necrotic black center. Rarely the primary sores are multiple. Two types of cases are distinguished, a mild type consisting merely of primary sore and satellite adenitis, and a severe type with the sore, adenitis, headache, rash, and fever of 10 days' duration, with aching pains, photophobia, toxemia, and even delirium. The rash is not characteristic. It appears about the fifth day being macular or papular, rosy or blotchy, diffuse or discrete, confined to the trunk or generally distributed, including the palms and soles. A bright red papular type of rash is common, and it comes out in daily crops. Though not itchy it is somewhat uncomfortable. General symptoms include a step-up fever, severe headache, stiff neck, aching, and restlessness. The fever drops on the tenth day. There are never sequelae, complications, or recurrence. The bubo does not suppurate. No specific treatment is known. See Pijper and Crocker (SoAfricaMJ 1: 613, 1938)

**Boutonneuse (Marseilles Fever)** caused by *R. conori* is closely related to Rocky Mountain spotted fever and may be identical with Kenya typhus. Infection is transmitted by the brown dog tick. The incubation period is 5 to 7 days, rarely as long as 18 days, and the onset is usually abrupt, with fever and repeated chills, headache and muscle pains, but comparatively slight prostration. A papular or maculopapular rash appears on the second to fourth day of illness, starting on the trunk, legs, and arms, and extending rapidly over the entire body, usually appearing last on the face. Volar skin is commonly involved. The soft palate may manifest small, round red spots for only a few days. The lesions, especially in dependent locations, may become petechial but seldom coalesce. A small ulcer presumably indicating the site of the infecting tick bite may be found early in the disease. It is only 2 to 5 mm. in diameter showing a black necrotic center surrounded by a red areola.

**Tsutsugamushi (Japanese River Fever, Kedani Fever, Scrub Typhus)** resembles the other rickettsial infections and is caused by *R. nipponica*. It is probably identical with Malayan scrub typhus, Queensland coastal fever and pseudotyphus of Sumatra. The larval forms of certain mites transmit infection to man from a reservoir probably in field mice and other rodents. The incubation period is from 7 to 21 days, generally a little less than two weeks. Prodromal symptoms occur as in typhus, and chilliness, headache and fever characterize the onset. Deafness is not a rare early symptom and joint pains and drowsiness are often present. Fever with perhaps considerable prostration, lasts about 2 weeks and falls to normal. The fatality rate approximates 15 per cent. The most characteristic sign is a small necrotic ulcer such as occurs in boutonneuse, and this is present in the majority of cases in Japan. It is not always found, however, in cases called scrub typhus in Malaya. General lymphadenopathy develops and is especially noticeable in nodes draining the site of

the primary ulcer which usually occurs in the pubic region, axilla, or leg. The typical rash of tsutsugamushi appears on the fourth to eighth day and consists of macules and slightly elevated rose-red or pink papules. It does not become petechial. It appears first on the trunk and face and extends to the legs and arms. It may be present on the palms and soles, and occasionally the face and the scalp are involved. The rash reaches its height in about 4 days and fades within 6 or 7 days. An enanthem may be present on the soft palate. Conjunctivitis and mild edema of the lids are usual (Ahlm and Lipshutz: J 124 1095 1944). Many patients show bronchial symptoms, sometimes with mucopurulent sputum, and pneumonia may occur as a complication. Hyperesthesia, pains in muscles and joints, deafness, apathy, clouded mentality, insomnia, and delirium may be encountered, Dyer wrote. Some immunity is conferred by an attack, but in some cases this lacks permanence. Para-aminobenzoic acid, given so as to maintain 30 to 60 mg per cent concentration in the blood, apparently reduces symptoms, morbidity and mortality (Tierney J 131 280 1946). See Chloromycetin p 155

Trench Fever is also known as five-day fever or Volhynia fever and is transmitted to man by the body louse. This disease disappeared after World War I. The incubation period varied from 5 to 20 days, onset was sudden with headache and pain in the legs, fever lasted about a week but frequently relapsed two or three times. A rash was present in the majority of cases, usually macular sometimes papular and was most commonly observed on the trunk. It sometimes disappeared in 24 hours. The disease was not fatal. It was controllable by eradication of body lice.

## RICKETTSIALPOX

**Symptoms.**—An initial lesion and a vesiculopapular type of eruption dermatologically characterize this interesting disorder which was recognized in an outbreak of previously unclassified disease which occurred in a Regency Park housing development in New York City in the summer of 1946. The initial lesion started as a papule rounded and firm, enlarging and undergoing central deeply seated vesiculation. The fluid was clear at first but became cloudy and the lesion shrank and dried so that a black eschar resulted. About one week after the start of the initial sore occurred the abrupt onset of chills, fever sweats, and backache coinciding with the height of development of the asymptomatic sore, which attained a diameter of 5 to 15 mm., with surrounding erythema but no induration. Regional lymph nodes were usually enlarged and slightly tender. The sore persisted for a total of approximately 3 weeks and usually left a small scar. The sore may not have been noted by the patient.

The onset of illness was sudden, with fever low at first but rising rapidly to 103° to 104° F with morning remissions for about a week defervescing gradually. Chills occurred in 70 per cent of the cases during the first days and were followed by drenching sweats. Headache was usual and severe and backache and myalgia resembled those of influenza. Lassitude was always present, photophobia sometimes and, less frequently soreness, dryness of the throat and nausea.

A rash appeared in all cases, usually being noted at the onset of fever or within a day or two later. The lesions were maculopapular discrete, and erythematous, the papules roughly circular firm, and sometimes surrounded by erythema. They ranged from 2 to 8 mm. in diameter and underwent summit vesiculation, simulating varicella, within a day or two. The vesicles dried, a black crust formed, and healing occurred without scarring. The rash was scanty moderate or abundant and was without pattern, though the volar skin was spared, and it endured usually for from 4 to 7 days. There was no physical sign of constitutional disease other than those associated with fever. There was no fatality. Moderate leukopenia with occasional relative lymphocytosis was observed. See Greenberg et al. (J 133 901 1947); Id. (AmJPubH 37 860 1947). The histopathology of the cutaneous lesions was described by Hersberger and Hoebner (PHRpts 62 1740 1947).

**Etiology**—The mouse mite, *Allodermanyssus sanguineus Hirst*, inhabiting the domicile of infected persons, was proved to carry the rickettsia, *R. akari*, which was shown to be the cause of the disease (Huebner et al.: PHRpts 61 1605 1946; 62: 777 1947) The house mouse was the probable carrier of the vector The organism was grown in the yolk sacs of fertile eggs and produced illness in mice and guinea pigs. A yolk sac antigen gave specific complement fixation tests with human convalescent serum. Agglutinations with *B proteus* $OX_{19}$, $OX_2$ and OXK were negative An interesting account of the finding of the mites by Pomerantz, an exterminator and Shankman, a physician is given by Roueché (The New Yorker Aug. 30, 1947 p. 23) See Sulzberger et al. (ADS 57: 767 1948)

**Treatment** was symptomatic. The disease apparently has been eradicated.

# DERMATOSES DUE TO BACTERIA

## STAPHYLOCOCCIC INFECTIONS

Staphylococci are often pathogenic (see Blair Bact. Rev 3 97 1939) In the skin, they can produce (1) epidermal infections such as impetigo, (2) intracutaneous and follicular infections such as infectious eczematoid dermatitis and furuncles, and (3) deep infections such as carbuncle, cellulitis, erysipelas-like lesions, abscesses, and gangrene. See Pillsbury (J 132 692, 1946)

Breed et al. (Bergey's *Manual of Determinative Bacteriology* Williams & Wilkins, 1948, p. 235) combine the genera *Micrococcus* and *Staphylococcus* and describe species of especial dermatologic interest among those which produce nitrites from nitrates but do not utilize $NH_4H_2PO_4$ as the sole source of nitrogen: *Micrococcus (Staphylococcus) pyogenes* var *aureus* liquefies gelatin, ferments mannitol and produces abundant orange growth on agar media; *Micrococcus pyogenes* var *albus* differs only in manifesting white growth; and *Micrococcus citreus* manifests yellow growth. *Micrococcus epidermidis* liquefies gelatin very slowly or not at all, does not ferment mannitol, and manifests a scant white translucent growth on agar media. These four species are aerobic to facultative anaerobic and do not produce pink or red pigment on agar media.

*Staphylococcus pyogenes* is the name that Bigger (BMJ 2: 837 1937) preferred for strains which hitherto have been known as *Staph. pyogenes aureus* and *Staph. pyogenes albus*; and he did not accept *Staph. citreus* as a distinct species. It was once thought that the activity of the staphylococcus is due solely to endotoxin, but it was shown that a broth filtrate contains toxin capable of killing rabbits when given intravenously Necrosis is produced by the subcutaneous injection of the toxin. Hemolysin was demonstrated and its presence in filtrates was recognized in 1901 leukocidin was also discovered early Burnet (1929) studying the cause of death from injections of contaminated diphtheria antitoxin, described the intravenous toxicity dermonecrotic effect, and hemolytic action of the exotoxin. Panton et al. discovered that intracutaneous injections of the exotoxin are immunizing. Pathogenicity Bigger noted, is usually associated with the ability of the strain to produce pigment. Defense consists in elimination by leucocytes or prevention of toxic effects by antitoxins. The necrotizing substance causes obstruction to the local lymph flow and so plays an important part in determining the histologic and physiologic aspects of the inflammatory lesion.

Staphylococcus toxin was the subject of an illuminating review by Rigdon (AmJMSc 199 412, 1940) There appears to be no relationship between the quantity of toxin produced and the virulence of the organism for man. The production of toxin by a given strain is not constant. Fractions described include leukocidin, hemolysin, acute killing fraction, dermonecrotizing fraction, nephrotoxin, coagulase and fibrinolysin. It has not been proved whether these fractions are the same or different substances. The antigenicity of conjugates of staphylococcus toxin with other substances, as noted on p. 28, is a phenomenon of unmeasured but perhaps great clinical significance.

Clarification of the properties of strains related to the dermatoses caused by staphylococci is by no means complete. No epidermonecrotizing agency has been described, yet pure cultures of *Staph. aureus* are often obtained from purely vesicular or bullous lesions.

The erythrogenic toxin in some strains produces a rash like that of scarlet fever (Aranow and Wood: J 119: 1491, 1942)

## STAPHYLOCOCCIC IMPETIGO

**Symptoms.**—Staphylococcic impetigo is an acute, superficial, usually primary, infectious dermatitis characterized by the rapid development of blisters filled with clear yellowish fluid appearing on normal-looking

skin or on top of red spots When the bullae enlarge, they become flat, sometimes with a depressed center They vary in size between that of a pea and a dollar piece or larger Differing from the ephemeral blister of streptococcic impetigo the bullae of staphylococcic impetigo usually persist for a period of days. After they have ruptured, the lesions become covered with thin, flat, varnishlike crusts of a gray or brown color easily distinguished from the thick crusts of the streptococcic disease. In older children and adults, the disease occurs chiefly on the face and neck. In babies the folds are preferred, neck, axillae and groins and lesions may develop all over the body, which may be covered with large readily rupturing bullae, a condition designated pemphigus neonatorum. Or staphylococcic impetigo may present circular or reniform lesions consisting of flat blisters and crusts about a zone centrally healed, so simulating circinate tinea (Epstein ADS 42 840 1940 44 317 1941 WiscMJ 40 353, 1941 )



Fig 169.



Fig. 170

Fig 169 —Circinate, probably staphylococcic, impetigo.
Fig 170 —Circinate, probably staphylococcic, impetigo (Dr J P Goeqalera)

Lesions appear singly or in crops. Itching is annoying, and scratching leads to autoinoculation The disease is typically a hot weather one, and accounted for no little morbidity in military personnel in humid tropical climates, where flexural (D Avanzo ADS 52 28 1945) as well as facial involvement was common.

Bockhart s impetigo is superficial staphylococcic folliculitis and is pustular from the onset Impetigo is a common complication of pediculosis capitis and scabies, as is also infectious eczematoid dermatitis. Impetigo of the buttocks is usually scabietic. Mucous membranes are sometimes affected by extension from the external sites.

Thick stuck-on crusts of yellowish, honeylike or dirty color and blisters of thin fragile walls, are typical of streptococcic impetigo (q.v p 171)

**Etiology** —Both staphylococci and streptococci have been recovered from impetiginoid lesions. Impetigo from the Latin an attack," is a clinical name devoid of etiologic connotation. Epstein, culturing

318 cases of impetigo, found only staphylococci in 166, only streptococci in 7, both organisms in 143 and none in 2 Carefully reviewing the findings of others, he noted that the particular bacteriologic technic influences the results. Mixed infections are common, as exemplified by the report of Cruickshank (Lancet 2 275 1941) who found in 23 cases Lancefield A streptococci in 15 and *Staphylococcus aureus* in 18. Epstein (JInvD 3 223 1940) fulfilled Koch's postulates by experimentally producing circinate impetigo with staphylococci See also Bigger et al. (BJD 56: 65 1944) whose selective cultural methods revealed staphylococci in 97 per cent of 130 patients, streptococci in 32 per cent, staphylococci only in 67 per cent, and streptococci only in 2 per cent

**Pathology**.—The epidermis is edematous and somewhat thickened. The roof of the bulla is formed by the stratum corneum. The cavity is filled with serum in which are found degenerated epithelial cells, leucocytes and a few lymphocytes. Numbers of cocci may be found these are likely to be at the border of the bleb. The dermis is inflamed moderately

**Diagnosis**.—In contact dermatitis the vesicles are small, closely grouped and itchy In pemphigus the eruption is not confined to the face, bullae develop as such, and the patients are adults. The presence or absence of pediculosis or scabies must be determined.

**Prognosis**.—Response to treatment is usually good. Fatal cases occur in babies. Reinfection may occur Autoinoculation prolongs the course. If scabies is present, it must be treated promptly and vigorously with temporary disregard of cocci If a case proves unduly rebellious, focal infection should be eradicated. In an extremely hot, wet environment, the disease may be practically incurable. Acute nephritis rarely complicates its relationship to medication is debatable (Silvers NYSJM 39 1093 1939)

**Treatment**.—One may wipe the lesions gently and anoint them liberally with a 2 per cent ammoniated mercurial paste, which should be reapplied several times daily Too strong an ointment is a mistake to be avoided. Sulfathiazole ointment has been highly recommended by Winer and Strakosch (J 118 221 1942) it is a hazardous sensitizer A microcrystalline sulfathiazole paste may cure overnight according to Harris (J 121 403 1943) Penicillin ointment, 500 units per gram in a lanolin and petrolatum base is comparatively tidy and often efficient. It should be applied at intervals of perhaps six hours, gently removing grease and débris with benzine prior to each fresh application. Ointments often fail We strongly recommend 2 per cent gentian violet in water Apply it daily only to exudative lesions and let the the surface remain dry Silver nitrate 10 per cent aqueous, is sometimes excellent but must not be repeated often enough to destroy the dermis. Compresses moist with 1 10,000 bichloride of mercury may beneficially be applied cool for 15 minutes 5 times a day Patients should be instructed as to the infectious nature of the disease and how to avoid autoinoculation

**Pemphigus Neonatorum** (R tt disease; neonatal dermatitis superficial coccic dermatitis in infants) is an impetiginous, usually staphylococcic, dermatitis in infants, in whom the infection i serious matter It may begin with localized redness, which gradually spreads until the major portion f the body is involved. Or t may begin with wrinkled, yellowish desquamating lesions, or easily ruptured bullae, or both, which appear in crops and spread widely Mucous membranes may be attacked. In the cases of Carter and Osborn (BMJ 1 465 1936) the laundry was the source of the infection, and areas touched by lens clothing were first affected. The desquamative process

may be severe, with the development of an oozing, eczematoid condition. Folliculitis, furuncles, and deep abscesses may develop. Constitutional symptoms are comparatively slight or wanting. Recovery or death generally ensues in from a fortnight to a month. The stools are loose, green, and contain *Staphylococcus aureus*. See Kendall and Aegerter (JPed 15: 733, 1939)

Cole and Ruh (J 63 1159 1914) are among the many who have confirmed the staphylococcic nature of the disease, which has nothing to do with the diet. The spread of organisms is subepithelial, a difference from the intraepidermal spread of the impetigo process. The absence of papillae in infants skins renders this easier than in adults Streptococci apparently caused the 4 cases of Cannon et al. (ADS 42: 834, 1940)

The pathogenic bacteria reach the infants usually from nasal carriers among the personnel who handle the children (Allison and Hobbs: BMJ 1, 1947)

**Prognosis.**—Almost half of v Rittershain's patients died. The outlook intimately depends on the treatment, which must be instituted promptly and must be appropriate. It is possible to inoculate staphylococci so widely by smearing a baby with grease that recovery becomes impossible Epidemics vary in virulence.

**Treatment.**—Prevention is possible when the source of infection has been determined. Aseptic, a nocleansing technic significantly reduced the incidence of impetigo neonatorum at the Philadelphia General Hospital (Ritter UOutRev 45: 460, 1941) Oily preparations are worse than useless, but the immediate and early evacuation of blebs, and the *careful* injection into them of 20 per cent silver nitrate have been reported effectual. Supportive measures are indicated. The 2 per cent aqueous solution of gentian violet is of great service. Hart (BJD 50 118 1938) used mercurochrome, permanganate baths and dusting powders he emphasized the necessity for opening the blisters and keeping the surface dry Undermined epidermis should be removed so that the antiseptic may have access to the place where it is needed Daily inspection is necessary Penicillin by injection saved the patient of Callaway et al. (JPed 28 592 1946) after other therapy failed. Penicillin ointment succeeded in 11 cases of Kendig and Firks (J 129 1094 1945)



Fig 171.—Neonatal staphylococcic exfoliative dermatitis, "pemphigus neonatorum." Fatal (Drs. Morrow Miller and Taussig.)

## INFECTIOUS ECZEMATOID DERMATITIS

**Synonyms.**—Pustular eczema (many cases) Impetiginous eczema (some cases) Superficial staphylococcic dermatitis.

**Symptoms.**—Infectious eczematoid dermatitis is characterized by erythematous, vesicular pustular or scaly circumscribed plaques of acute dermatitis which commonly develops from staphylococcic complication of a minor injury to the skin The exposed parts are those generally first affected. The initial lesion may be a vesicle pustule, or an inflammatory scaly or crusted papule The vesicles are not so closely placed and are larger than in an acute vesicular contact dermatitis. The lesions are asymmetric as a rule. The eruption spreads by autoinoculation and occurs in circumscribed patches of moderate size which enlarge by peripheral extension Vesicles soon break to form an oozing patch which extends. New foci begin as a cluster of vesicles. The epidermis at the periphery of the lesion is usually undermined, detached or raised by



Fig. 172.



Fig. 173.

Fig. 172.—Infectious eczematoid dermatitis (Sutton J [illegible] 1930)
Fig. 173.—Infectious eczematoid dermatitis. (Dr. Gosquierre.)



Fig. 174.



Fig. 175.

Fig. 174.—Infectious eczematoid dermatitis of palm.
Fig. 175.—Infectious eczematoid dermatitis, showing vesiculation, leucocytic infiltration of epidermis and dermis, and disruption of corneum.

collections of seropurulent fluid which may contain much fibrin so that a thin, ridgelike crust forms about the periphery There is no tendency to involute centrally Itching is usually considerable. There is usually lymphadenitis, particularly when the disease is widespread, as it may be even to the extent of being universal. The disease is often associated with scabies, pediculosis, furunculosis, otitis, or other suppurative disorder such as an infected ingrowing toenail. It is commonest in active adults.

**Etiology**—Engman (AmM 4 769 1902) recovered the staphylococcus in pure culture from early lesions and from the surface and crusts of later patches. Experimental autoinoculation can usually be performed then the lesion begins as an erythematous patch which soon becomes moist and crusted. It is thought that allergy plays some part (Foerster WiscMJ 34 305 1935) The chronicity and rebelliousness of infectious eczematoid dermatitis distinguish it from ordinary primary staphylococcal infections and convince us that more than a primary infection must be concerned. Contact dermatitis is often the primary disease, and contactants may require elimination before antiseptics attain lasting effectiveness. Foci of infection are also frequently concerned. Dermatitis of the hands, an intractable and disappointing disease according to most medical literature, has proved to be usually gratifyingly responsive if the aspects of contactants and foci are adequately dealt with (see Lane et al. J 128 987 1945)

**Pathology**—The papillae are swollen and congested There are slight acanthosis and edema of the prickle cells. Destruction is marked in the lowest layers of the stratum corneum, which is undermined and detached, and its elevated margins are frayed Abscesses are to be found in the upper region of the rete and groups of cocci can be seen in them. Polymorphonuclear leucocytic infiltration is profuse

**Diagnosis.**—In contact dermatitis, the eyelids are usually swollen and itchy and the flexures are involved by predilection The disease is not primarily pustular but by secondary infection often is complicated by infectious eczematoid dermatitis. The impetigos occur generally in children their lesions are discrete, and seldom involve the body and limbs. Staphylococcic impetigo differs little from infectious eczematoid dermatitis Perhaps one may say that staphylococcic impetigo in the presence of contact dermatitis or focal infection is identical with infectious eczematoid dermatitis The discrete pea to fingernail size, deeply seated, painful, not itchy pustules and crusts of ecthyma are distinctive Moniliids and other myceids must also be differentiated They too may be complicated by staphylococcic parasitism

**Treatment.**—Greasy preparations are to be avoided especially irritating ones, such as sulfur ointment A 2 per cent aqueous solution of gentian violet is of considerable value Cole recommended the use of hot 1.5 000 aqueous solution of potassium permanganate 20-minute soaks 3 or 4 times a day for 4 or 5 days Radiant heat is useful. Gentle débridement is an important part of treatment Crusts must be removed so that antiseptics can reach the bacteria. Baths in bichloride of mercury 1 10 000 (4 gm in 10 gallons of tepid water) are useful and comforting but one must be alert to percutaneous absorption and mercurial intoxication (diarrhea) when bichloride baths are used. Wet packs of bichloride may be laid over lesions painted with gentian violet, with satisfactory re-

sults, especially when both staphylococci and streptococci are present, as they often are. Foci of infection must be eradicated in resistant cases teeth gums, sinuses, prostate, and running ears are the commonest of these. Hospital care is much to be preferred to ambulatory

Penicillin in large intramuscular dosage is quite efficient. A common experience is to give penicillin with temporary benefit, only to observe relapse soon after it is stopped. When this happens, one may be confident that focal infection is significant. Contact irritation must also be eliminated. Chronic pustular dermatitis of hands and feet can usually be cured when approached from this standpoint. Hopkins and Burky (ADS 49 124, 1944) reported successful desensitization by intracutaneous immunization with staphylococcus toxin Cooper (PaMJ 46 218 1942) also eliminated foci and used staphylococcus vaccine Bacitracin ointment, 480 U per gm., rarely irritates and often benefits (Miller et al.: JInvD 10 179 1948) X ray therapy is only rarely helpful. When vesicular dermatitis is not responsive to x ray staphylococci are probably causative.

**Jungle Rot** was the G.I name for this disease in the tropics, where heat, humidity and staphylococci, along with other factors perhaps, such as hygiene nutrition and quinacrine, produced much morbidity during World War II (Travis Mil Surg 97 224 1945 Cohen USNM Bull 42 1119 1944)

## FURUNCLES AND CARBUNCLES

**Furuncles (Boils)** are acute, circumscribed, follicular phlegmonous inflammatory lesions caused by virulent staphylococci in the skin. Carbuncles are complex furunculoid lesions involving not only the skin but also the subcutaneous tissue, with suppuration sloughing, and the discharge of necrotic material through multiple openings.

In a furuncle, the inflammatory process begins as a rule in the immediate vicinity of a skin gland or hair follicle. Furuncles may number from 1 or 2 to 50 or more, and disease may be prolonged almost indefinitely by repetitious development of new lesions. The neck, axillae, face buttocks, and legs are sites of predilection, although no region is exempt. A lesion begins as an itchy acuminate pustule surrounding a hair As it develops, the involved skin becomes smooth tense and shiny painful and tender In a few days the tumor usually matures, and either comes to a head or becomes boggy and fluctuant. In some cases regression takes place before the occurrence of suppuration, and the lesion a blind boil, slowly undergoes absorption On reaching maturity a boil generally ruptures spontaneously and a necrotic core is discharged, together with pus and serum. Healing speedily ensues. In some boils the center undergoes necrosis but becomes tough, stringy and tenacious. Such boils are of relatively small size extremely painful and less responsive to treatment than ordinary ones. They are due to strains of staphylococci which produce necrotizing toxin

**Carbuncles** resemble furuncles but are larger and are accompanied by more or less systemic disturbance. When necrosis occurs, their contents are discharged through several openings. The lesions are commonly single. They start with painful localized erysipelas-like induration, which gradually increases in size The affected skin is dark red, tense and shiny Suppuration occurs within from 7 to 14 days, but instead of a

single central slough as in a furuncle, the tumor drains through a number of openings and the purplish summit presents a cribriform appearance. The central portion of the lesion may undergo necrosis at several different points at the same time, and a number of small sloughs form and are cast off or the entire mass may be involved at once, with the resulting formation of a deep ragged ulcer This cavity fills up with granulation tissue and ultimately heals with more or less scarring Systemic intoxication may be severe even fatal and metastasis and septicemia are possible complications. The sites of predilection are the neck, shoulders, buttocks, and outer surfaces of the thigh



Fig 176



Fig 177

Fig 176 —Furuncl of the back. (Dr George M MacKee)
F g 177 —C buncl of eck.

**Staphylococcic Abscesses and Cellulitis** require mention.

**Etiology** —Pasteur in 1880 described the cultivation of microorganisms from a boil

A puncture was made at the base of the small cone of pus at the apex of a furuncle on the nape of the neck. The fluid obtained was at once sowed. The next day the culture fluid had become cloudy and contained a single organism, consisting of small spherical points arranged in pairs, sometimes in fours, but often in irregular masses. He demonstrated the pathogenicity of the germ he had cultured and recovered it from lesions produced by cultures in human volunteers.

The appearance of new lesions is not ordinarily due to septicemia, but follicles are infected exogenously Ointments facilitate autoinoculation. Crops of semiglobular lesions developing umbilicated necrotic centers, representing bacterial emboli and liquefaction necrosis and resembling acne varioliformis, were described by Balog (JInvD 5 107 1942) and attributed by him to metastasis from a primary suppurative focus.

Certain factors predisposing to microbic invasion are generally recognized Of these diabetes mellitus, nephritis, and avitaminosis are the most important. In every case of furunculosis the patient s urine should be examined. Occupational exposure to grease such as cutting oils also predisposes, but furuncles, which multiply should be distinguished from

oil acne, which is associated with comedones (Schwartz PHRpts 56 1947 1941) Warmth humidity and sweating render the skin especially vulnerable to staphylococcic parasitism, for they interfere with self-sterilization by drying In obstinate cases, search should always be made for foci of staphylococci in sinuses, tonsils, teeth, and urogenital tract. The influence of vitamins is apparently consequential only in their decided lack, although vitamins A, $B_1$, and C may have some therapeutic usefulness.

**Pathology.**—The inflammatory process involves a gland or follicle. The slough is composed of pus, fibrin and necrotic glandular and periglandular tissue Changes in the dermis are those of acute, purulent inflammation. In carbuncles, the infection is deeply seated, and the dermonecrotizing inflammatory process involves dermis and subcutaneous tissue.

**Diagnosis.**—The staphylococcus is readily found in the pus and may be cultivated easily Erysipelas is not pustular Anthrax is characterized by vesicles about a blackish, necrotic center Syphilitic lesions are less acute and painful by far

**Prognosis.**—Recovery generally ensues within a few weeks. Lesions involving the face or scalp are especially dangerous. In elderly and debilitated individuals, a virulent infection may prove fatal. The disease usually responds favorably to treatment, although recurrences through autoinoculation are common.

**Treatment.**—Morphine or codeine may be required and should not be withheld. The urine and blood sugar should be tested. The value of vitamin preparations is highly debatable. Thyroid was given by Barnes (JClEndocr 3 243 1943) who explained his favorable results on the basis of improved skin temperature tone, and circulation. The only oral medication the senior author used to prescribe was sodium citrate In adequate amounts it tended, he felt, to hasten necrosis and liquefaction Sulfonamides have been recommended, but chemotherapy alone is inadequate when there exists an accessible collection of pus, which, as John Hunter taught, must be let out (Beling and Abel AmJSurg 50 258, 1940) Osgood (JPed 17 740 1940) claimed benefit from neoarsphenamine and sulfathiazole Passive immunization by means of antitoxin has been tried. Stookey and Scarpellino (SMJ 32 178 1939) investigated dermonecrosis and were able to help some cases by giving antitoxin. It has value in toxic cases. Bacteriophage is well thought of by some authors It may be applied as a moist compress. We do not use it. Vaccine therapy gives as satisfactory results in furunculosis as in any bacterial disease in which it is used. The preparation probably should be autogenous. We do not use vaccine plasters.

Dermonecrotizing toxin produces necrosis quantitatively related to the amount of toxin injected It is neutralized by simultaneous injection of immune serum. Denatured with a small proportion of formol so as to form toxoid, it does not produce necrosis. Toxoid injections evoke active humoral immunity to toxin without causing severe reactions. A course of toxoid therapy is often highly efficacious (Zernetol Surg 17 363 1945) although the staphylococcus antitoxin titer is not of much clinical utility

Penicillin by injection is often eminently satisfactory The dose should be large. Some strains of staphylococci are not responsive, and some cases of chronic furunculosis improve only temporarily If a given dosage does not yield results, one should increase it greatly before assessing the

agent as useless in that case. Since penicillin does not influence immunity toxoid should be given also we believe Penicillin ointment is not especially valuable in general, but is helpful in furunculosis of the scalp in infants, Dennie tells us.

Mild antiseptics applied in the form of blotterlike moist poultices may be employed. A good plan is to paint the lesions and their periphery once daily with diluted tincture of iodine or 1 per cent gentian violet in alcohol to prevent autoinoculation then to apply a large gauze pack moistened with half and half glycerol and alcohol. Incandescent lamps, 500 c.p are of value as a source of radiant heat especially in early stages. Ultra violet light is worthless in this condition. Rest and local isolation are important. Incision must not transgress the protective zone. If the patient is toxic, give antitoxin In recurrent cases, find the focus of dissemination of the virulent germs, this focus may be inconspicuous. There seems little doubt that susceptibility is variable for some individuals are infected time after time and others rarely suffer Immobilization is important, and this may be accomplished in small lesions by the use of collodion, protective dressings, and perhaps a *sling* Fraser (*BMJ 2 894 1935*) recommended an elastoplast occlusive dressing which protects, relieves pain, and enables a patient to continue his work.

Roentgen therapy has been discussed on page 55 The effect of electromagnetic energy is not on the organism. It is usual to give small doses. The more acute the lesion the smaller the dose Epstein teaches But on the back of the neck and in the axilla MacKee pointed out, one suberythema dose may prevent the development of new lesions. It may be necessary to depilate the parts in order to effect a cure, and this should be accomplished with fractional doses, avoiding erythema. Soon after the treatment the patient is likely to be worse but within 48 hours the pain will have disappeared In some cases the induration is gradually absorbed, while in others the lesion softens and discharges. When the lesion is treated before discharge and while in the indurated stage, x rays cause rapid regression. X ray treatment of lesions of the face is curative, painless, and safe, with much smaller morbidity and mortality rates than surgery yields (O Brien NEngJM 220 917 1939) Cannon (SMJ 38 106 1945) recommended the following measures 400 to 600 r radiotherapy including a good margin daily irrigation of the region with 5 per cent phenol a thick cotton dressing embodying a paste composed of fluidextract of ergot 6 0 phenol 0 6 and zinc oxide and starch 4 0 of each in cold cream the probing of openings with 50 per cent phenol and intramuscular injections of colloidal manganese or sterile milk

A boil can perhaps be aborted by the early local application of mercurial plaster or of tincture of iodine One may hasten its maturity by the aid of hot, moist, antiseptic dressings.

Many authors have insisted that a boil should never be incised. There are exceptions to this generally wise rule A tiny itchy and painful follicular pustule will progress considerably unless it is aborted. If the point of a scalpel is moved through the undermined epidermis across the follicle mouth so as to penetrate *something less than half of the thickness* of the corium drainage will be made adequate A drop of tincture of iodine is then applied and the lesion left dry Extraction of the infected hair is an error for this procedure gives the staphylococcus free access to subdermal spaces, where an abscess is the least of the prognosticable evils. It is especially dangerous to extract infected vibrissae. Squeezing a lesion accomplishes the same bad effects.

A surgical attack upon carbuncles is occasionally to be recommended. Prior to penicillin, crucial incision in the early stage was popular a radical effort being made under gas or pentothal anesthesia. The flaps were laid back, the pockets cleaned out, and the wound packed with moist iodoform gauze or similar material. Complete and early excision of the infected mass has been advocated but this is rarely necessary Conservative treatment in contrast with surgery led to lower mortality rates, lower morbidity rates, and better cosmetic results (Ayres et al. J 108 858, 1937) Excision of a carbuncle may stop pain and intoxication dramatically

## OTHER STAPHYLOCOCCIC DERMATOSES

Folliculitis is often staphylococcic, differing from furunculosis mainly in depth and severity of inflammatory reaction about the hair or sebaceous follicles. A solitary lesion, itchy acuminate and pierced by a hair may comprise the whole disease; or such lesions may affect a considerable area or may be widespread over the hairy regions of the body Sycosis is described separately (p. 675) It is not remarkable when the infection penetrates to the subcutaneous layer so that an abscess develops. This is often seen on the dorsa of the fingers, and the lesion may have a collar button shape

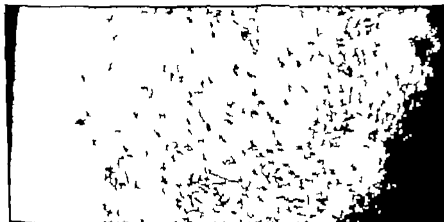


Fig. 178.—Folliculitis Bockhart' impetigo.



Fig. 179.—Hemolytic Staphylococcus aureus productive of disease simulating Paget carcinoma.

with a small purulent bleb on the surface a tiny hole through the skin, and a pocket of pus beneath requiring incision and drainage. Folliculitis often results from autoinoculation, especially as the result of smearing staphylococci about by the application of greases. When folliculitis is chronic, focal infection must be sought out and eradicated. The usual antistaphylococcic measures as for furuncles are applicable.

**Rosacea like Folliculitis** is a clinical entity which we have not seen described elsewhere. It closely resembles rosacea, but may be quite itchy which is a difference and the shallow pustules, surrounded by considerable erythema, may be recognized as follicular when examined under magnification. This chronic disease may be discrete or confluent. It responds to penicillin in oil in large doses and to elimination of foci, usually oral, occasionally genitourinary. Vioform ointment may be helpful.



Fig 180—Pyoderma Faciale (Cole and Driver ADS 41 572, 1941.)



Fig 181—Acne necrotica miliaris the tiny itchy follicular lesions are probably coccic in origin (Montgomery ADS 36 40, 1937)

**Pyoderma Faciale** was described by O Leary and Kierland (ADS 41: 451, 1940) as an explosive eruption of deep pustules on the face in young women who perhaps have not had preceding acne. Tunneling abscesses, thick greenish pus, pain and tenderness, and disfiguring keloidal scars are characteristic. *The patient* is often underweight, anemic and amenorrheic but tuberculosis has not been found. Antianemic and vitamin therapy appear to be indicated. X-ray therapy may be used. Very large doses of penicillin may do the job when modest ones do not. Compare Hidradenitis axillaris suppurativa (p. 693)

**Acne Necrotica Miliaris** of the scalp is a form of folliculitis which constitutes a typical clinical entity and which is probably due to staphylococci. The patients are generally of middle age. The lesions are discrete, isolated, and itchy. Pruritus is intense, being disproportionate with the visible disease. There may be perhaps 10 to 100 lesions. Before excoriation, which is their prompt complication, they are tiny vesicopustules. Perhaps because of excoriation, they leave little scars. If the disease persists and is persistently excoriated, the hair may become thin as a result of alopecia cicatrisata. Seborrhea plays no important role in etiology. Montgomery (ADS 36: 40 1937) demonstrated ulceration between adjacent hair follicles, with a serosanguineous crust and a moderate infiltration mainly of lymphocytes extending into the mid cutis. Numerous staphylococci were seen at the margins of the ulcer. Applications of ammoniated mercury may cure these patients. Staphylococcus toxoid, penicillin by injection, and eradication of foci of infection, especially prostatic, are effective measures.

## STREPTOCOCCIC INFECTIONS

A basic serologic classification of *Str. pyogenes* (equivalent to group A hemolytic) was made by Griffith (JHyg 34: 542, 1934). See Lancefield and Hare (JExpM 61: 335, 1935) regarding classification. The epidemiology of streptococcic infections was well delineated by Bradley (BMJ 2: 733 1938). See Mackie (EdinMJ 47 466, 1940) regarding herd infections. When any part is infected with streptococci, pathogens are plentiful as transients on healthy areas (Martin BMJ 2 243, 1942).

*Str. viridans* and nonhemolytic streptococci, apart from rare strains, are of little significance as human pathogens. One strain of *Str. pyogenes* may in any given epidemic produce angina, scarlet fever, erysipelas, cellulitis, lymphangitis, adenitis, otitis, sinusitis, meningitis, puerperal fever and septicemia, in accordance with the unitarian hypothesis. Therefore the tendency is to discard specific names for strains which depend on morphology and cultural characteristics. Most hemolytic streptococci are identifiable by a specific carbohydrate substance and fall into Lancefield's Group A. This group was divided into about 30 subtypes by Griffith. Bradley described single-strain epidemics in various semi-isolated groups. The rash of scarlet fever is fortuitous, he stated, but each type of the disease, streptococcic infection, is an index of the prevalence, and an indicator of the existence of the pathogen in the community. The aggregate of the clinical manifestations probably represents about half of the actual streptococcic morbidity. The great bulk of streptococcic disease is probably symotic and associated with an increased carrier rate, enhanced parasitism being at any given time due to one or few serologic types of the organism. Droplet infection is common, as well as milk borne, but comparatively intimate contact is required, less important is casual contact. The tempo of transmission is slow and is due probably to transference via immune carriers. A period of from 5 to 10 days elapses between infection and detection of it. Immune carriers are probably infected for only a brief period, but these are probably more important epidemiologically than persons with chronic foci. A type-specific epidemic runs its course and dies out spontaneously. Persistence of the incidence of infection and recurrences points to the introduction of a new type of streptococcus.

## STREPTOCOCCIC IMPETIGO

**Symptoms.**—Streptococcic impetigo is characterized by superficial lesions covered with thick crusts of a yellowish, honeylike color according to Epstein (WiscMJ 40 383 1941). Compare staphylococcic impetigo, p. 159. The streptococcic disease starts as a red spot, on top of which a thin-walled blister develops, and this may so rapidly collapse as to be missed. In simple cases a few crusted lesions are present. In severe cases the lesions become confluent so that the face may be covered by masses of discharging eroded crusts, the original yellow color perhaps changing to a dirty brown from admixture with blood. Regional lymphadenopathy may occur. Being superficial, no scar remains after healing, although macular pinkish or brownish staining may persist for some weeks. The favorite location is the face, but the neck, hands, and scalp are also frequently affected. Any location may support the infection, especially when it is secondary to another dermatosis. On the fingers or toes, where the

corneum is thick, one finds rapidly enlarging painful bullae, which the dermatologic consultant often sees after the patient has erroneously been treated for tinea. The latter itches rather than hurts, and its progress is less precipitate.

Ecthyma involves dermonecrosis, and is related to streptococcic impetigo as furuncles are related to staphylococcic impetigo

**Etiology**.—Streptococcic impetigo occurs either as a primary disease or as secondary infection of any itching dermatoses such as scabies, der



Figs. 182 and 183.—Impetigo contagiosa.



Fig. 184



Fig. 185.

Fig. 184.—Impetigo bullosa, severe (Dr Katron.)
Fig. 185.—Impetigo of fingers.

matitis venenata, or infantile eczema. As a primary disease its incidence is seasonal maximal in the fall and parallel with other streptococcic diseases. Comparatively close contact is requisite to transmission. The organism is hemolytic. Mixed infections with both streptococci and staphylococci are common.

Treatment.—The principles involve gentle débridement and isolation of the lesions, the use of suitable antiseptics, and prevention of autoinoculation and spreading. Ammoniated mercury ointment, 2 per cent, removed by benzine at the times when it is refreshed, is often effective. Sulfonamide ointments, if they are ever used, are useful here. Penicillin ointment, 250 to 1 000 units per gram, may yield a 24- or 48-hour cure. Penicillin by injection may be of value in difficult or extensive cases. See also treatment of staphylococcic impetigo and infectious eczematoid dermatitis.

## ECTHYMA

Symptoms.—Ecthyma is manifested by the formation of small, discrete, flat, painful pustules, which heal reluctantly and may be followed by slight scarring and pigmentation. A child is the usual patient. The legs and thighs are the sites of predilection, although no region is exempt.



Fig. 186.



Fig. 187

Fig. 186.—Ecthyma, showing typical lesions of the leg.
Fig. 187.—Erysipelas of face.

The lesions, ranging in number from 1 to 20 or more, are irregularly oval sharply defined, and have reddish areolae. They begin as small yellowish, pustular excavations, which enlarge. The exudate desiccates, forming thick, adherent, brownish crusts. The bases are raw and tender. On healing the crusts drop off, but the disease may be continued indefinitely by the development of new lesions. Slight lymph node involvement is usual. The lesions sometimes persist for weeks, unless correctly treated.

Etiology.—Streptococci perhaps complicated by *Staphylococcus aureus* are the usual agent. Uncleanliness, poor hygienic surroundings, and

inadequate diet are also concerned. Trauma and insect bites are the exciting causes as a rule. The disease is readily autoinoculable.

**Pathology**.—The lesions are shallow abscesses The dermis is swollen, infiltrated, and perhaps necrotized. Purulent inflammation and exudation are seen in sections.

**Diagnosis**.—In flat pustular syphilids lesions are more numerous and disseminated, edges of ulcers are abrupt, there is little pain, and crusts are bulky and greenish while other signs of syphilis are usually apparent.

**Treatment**.—As a rule the disease responds favorably to sulfonamide treatment. Prior to sulfonamides and penicillin, these cases were extremely stubborn Débridement by gentle measures is important with a view to the avoidance of autoinoculation. An antiseptic such as 2 per cent tincture of iodine may then be applied Bichloride of mercury 1 10 000, in wet applications is excellent. Scratching and picking at the lesions must be prohibited Fractional unfiltered radiation in small doses usually helps. Sulfadiazine by mouth, applying nothing topically is generally promptly curative Penicillin injections, along with permanganate baths, are efficient when sulfonamides are inadvisable Penicillin ointment was recommended by Wright and Gross (ADS 55 52 1947)



Fig 1?? —Streptococcic dermatitis.

## STREPTOCOCCIC DERMATOSES

**Synonyms**.—Streptococcic impetiginization subacute and chronic impetigo intertrigo (some cases) streptococcic fissure streptococcic epidermitis pityriasis simplex (some cases) pityriasis streptogène; seborrheic eczema (some cases)

**Symptoms**.—The streptococcus can cause persistent, scaling and oozing inflammations which tend to undergo fissuring and which are painful and stubborn in response to treatment especially wherever folds or flexures are involved (Chipman ADS 4 526 1921)

Impetiginization may follow impetigo, or it may develop as streptococcic infection superimposed on and secondary to dermatitis of various causes. Banal irritation or comparatively inconsequential dermatitis

venenata is occasionally so infected, particularly when it is located in a fold or flexure where the skin is moist. All stages of dermatitis are seen, ranging from crusted, oozing areas to dry scaly patches. Fissures are especially common behind the ears (spectacle frames and perspiration abet this) at the angles of the mouth, and at the anterior angle of the naris. Fissure of the lip (p 718) is usually streptococcic.

Pityriasis Simplex, the chronic, dry type, is seen usually on the face in the form of furfuraceous patches, practically asymptomatic excepting the branny desquamation. Behind the ears the dermatitis is likely to present a red and weeping surface, glazed and covered with exudation. Dry scaling may involve the the ear canal (Williams et al. J 113 641 1939) The whole scalp and neck may be affected in widespread cases. Circinate, furfuraceous patches of the face in Negroes, producing depigmentation, were called erythema streptogenes by Dobes and Jones (ADS 53 107 1946)

Etiology.—While hemolytic streptococci are often found in impetigo nonhemolytic organisms are the ones found in streptococcic intertrigo (Kinnear BJD 48: 173 1936 Mitchell ADS 19 659 1929 40 635 1939 J 108 361, 1937) It is wise to make smears and cultures of oozing dermatoses, for the findings affect one s choice of therapy

**Prognosis and Treatment.**—The duration of these disorders may be prolonged. They are resistant to treatment by ill-chosen or irritating measures. Weak ammoniated mercurial paste (2 per cent) removed with benzine and refreshed twice a day may help Sabouraud used 1 per cent iodine in alcohol. Lotions and wet compresses are preferable to ointments, although sulfanilamide ointment has been effective. Bichloride of mercury (1:10 000) is effectual. Aqueous solution of gentian violet may be applied daily but it is sometimes ineffectual. Penicillin ointment may yield prompt cures. Débridement, gently performed, is essential to success. X ray therapy has only a little value in temporarily diminishing the swelling, redness, and pain. All involved regions must be treated at the same time, for a nostril will not heal if an infected postauricular area is neglected. In cases affecting the corners of the mouth, the teeth must be freed from calculus, decays repaired, pyorrhea adequately dealt with, and dead and abscessed teeth removed. In streptococcic aerodermatitis Mitchell found correct diagnosis the fundamental requirement, distinguishing fungous infections and dermatitis venenata, and utilizing weak bichloride of mercury soaks and ammoniated mercurial ointment in cases in which streptococci are identified. Our experience confirms reports of benefit from sulfonamides. Penicillin by injection is especially valuable in severe cases. Focal infection must be sought out and eradicated.

## ERYSIPELAS

**Symptoms.**—Erysipelas is an acute, localized, polymorphonuclear cellulitis due to streptococci when they involve skin and subcutaneous tissue. It is characterized by redness, edema, and induration, accompanied by intoxication. Cutaneous manifestations are generally preceded by feelings of malaise and chilliness followed by fever The eruption begins as a small erythematous patch which gradually enlarges, the involved skin becoming swollen and indurated, pinkish or reddish, hot and tender with a glazed surface on which bullae occasionally develop. Margins of the patch are sharply defined from the first, and lesions usually spread grad-

ually by peripheral extension. Local symptoms are seldom severe, but there are some burning and itching Lesions are generally single and seldom involve very extensive areas. Two or more discontinuous regions of activity may be seen, in rare cases. The extent and rate of spread are measures of the severity of the disease. In infections of little virulence and slow rate of spread the central zone may clear as the periphery slowly expands. The face is a site of predilection, although no region is exempt. There may be considerable swelling and edema, particularly in cases involving the face and ears. The mucous membranes sometimes are attacked. Occasionally a case is seen in which the inflammatory process is confined almost exclusively to the subcutaneous tissue edema of the overlying skin being the sole superficial manifestation.

An attack uninfluenced by treatment generally lasts from one to several weeks, and fever is usually present throughout the course. Within a few days or a fortnight the process reaches its acme, then persists unchanged for a time, and finally begins gradually to subside As involution takes place, the dusky red color slowly fades to a brownish and then a yellowish hue, and ultimately the epidermis regains its normal color There is always more or less desquamation.

**Etiology** —Spink and Keefer (JClinInv 15 17 21 1936) in a study of 30 cases found β-hemolytic streptococci in the lesions or in the nasal secretion of all cases. *Streptococcus pyogenes* produces (1) streptococcic hemolysin, (2) streptococcic leucocidin (3) an erythrogenic toxin, (4) a fibrinolysin, and (5) a substance which increases skin permeability and these aggressive substances somehow determine its pathogenicity Perhaps antitoxic immunity which is the essential factor in resistance to scarlet fever is relatively ineffective as a protection against *Str pyogenes* invasion of the skin, the essential feature of erysipelas. While the erythrotoxin may play a part in the disease, it seems that the degree of antitoxic immunity which will protect against scarlet fever will not protect against erysipelas.

**Pathology**—There is fibrinous and leucocytic exudation throughout the dermis. Blood and lymph channels are dilated and congested. There is marked perivascular infiltration, consisting mainly of polymorphonuclear leucocytes. The prickle cells are swollen, cloudy and vacuolated. Colliquation necrosis is usual. Streptococci are found chiefly in the lymphatics but are also distributed in the tissues The inflammation, violent as it is, completely resorbs with no cicatricial sequelae

**Prognosis**.—In 1,193 cases (Hoyne MRec 141 132, 1935) the mortality was highest in the first year of life (39 per cent) and in old age (43 per cent in the 76- to 85-year group) The pregnant patient developing erysipelas is likely to abort within 24 hours (Lynch ADS 26 997 1932)

Fatal cases, according to Toomey (AnnIntM 12 166 1933) occurred generally among (1) infants less than 1 year of age, (2) patients more than 60 years of age, (3) patients with pulmonary disease such as tuberculosis and pneumonia, (4) patients with chronic organic disease such as myocarditis and arteriosclerotic disease, (5) patients with concomitant acute infections, (6) patients who had a severe debilitating illness immediately before their erysipelas (7) patients with alcoholism, and (8) patients who had suffered severe injury Not all patients in these groups die but all of the patients of Toomey series who died belonged to one of these.

In 160 cases seen in Panama (Miller et al. BMJ 35: 757, 1945) 46 were primary and 2.5 per cent died. Whites were 4 to 5 times as susceptible as natives. In addition to local lesions, other manifestations in order of incidence were chills, local

lymphadenitis, vomiting, headache, aching anorexia pharyngitis, diarrhea, convulsions icterus, distention, delirium, toxic psychosis, and orbital abscess.

**Diagnosis.**—Erysipelas is to be distinguished especially from erythematous contact dermatitis. The marginated indurated lesions and the fever and malaise which always accompany them are distinctive.

**Treatment.**—Morphine may be used freely Good nursing care is of great importance. Bed rest, the urging of fluids, and alkaline diuretics are usually ordered. It has become common knowledge (J 108 32, 1937) that sulfonamides possess remarkable properties in the cure of streptococcic infection and in diminution of its complications. With their use, lesions of erysipelas become dusky red and purplish within the first 12 to 24 hours and disappear completely within from 4 to 10 days. Inflammation resolves, symptoms improve, and fever falls almost at once. One should institute treatment early Sulfanilamide reduced hospitalization time from 11 to 7 days in the experience of Nelson et al. (J 112 1044, 1939) It reduced mortality rates as compared with antitoxin from 9.2 per cent to 1 6 in adults, and from 37.5 per cent to 12.9 in children. Treatment other than sulfonamide was adjudged obsolete by Shank et al (J 117 2238, 1941) in whose experience no lesion spread after 36 hours of chemotherapy while only 10 per cent of the patients were febrile after 4 days. We give both penicillin and sulfadiazine.

A dose of from 75 to 150 r of unfiltered x ray therapy may be given over the affected area and a margin of 2 inches of surrounding normal skin as early in the course of the disease as possible, and followed by the same dose the next day Ultraviolet ray treatment of the lesion and a surrounding zone of uninflamed skin is said to be of value, twenty times the erythema dose being recommended by Titus (BJPhysM 9 160 1934)

Antistreptococcic serum has been proved beneficial and should be given a trial in extremely toxic cases. The dose is from 10 to 20 c c of a reliable concentrate intramuscularly at 12 to 24-hour intervals.

No local medicament reaches the subepithelial region of activity Continuous warm packs are more or less comforting the solute being inconsequential if it is nonirritating Ichthyol ointment is popular but inert

**Recurrent Erysipelas.**—Relapses may occur within a few hours o days after apparently complete dissipation of the disease, or after months or years, Andrews noted (Dis. Skin, Saunders, 1946) Antistreptococcic therapy should not be discontinued too early Chronic recurrent erysipelas constitutes a characteristic entity resulting in persistent lymphedema and elephantiasis. This rebellious and disfiguring disease, to be distinguished from the erysipelas-like dermatophytid (pp. 311, 363) may respond to elimination of foci of infection and immunization with streptococcus toxin (Stevens J 100: 1764, 1933) Andrews recommended also penicillin ointment, plastic surgery and x ray therapy Penicillin, x-ray and solid $CO_2$ did not help a case of Ormsby's (ADS 57 463, 1948) O'Leary discussing this patient, advised a search fo portals of entry of infection, the use of rubber bandages, vaccines or sulfonamides prophylactically and perhaps the injection of boiling water into the edematous area, which results in severe reaction, occlusion of lymph vessels, and decrease in edema

## SCARLET FEVER

**Symptoms.**—Scarlet fever is an acute, febrile streptococcic infection usually of the throat, characterized by a toxic rash which is diffuse, brightly erythematous, and productive of desquamation The incubation period as a rule is short. Headache, anorexia, and vomiting are frequent early symptoms. High fever and a sore throat, which may present simple inflammation follicular tonsillitis, or a white diphtheroid membrane, are

typically abrupt in onset. Regional lymphadenitis is painful and suppuration is not a rare complication. The throat is at first dry but later becomes congested, raw and exceedingly tender. The buccal mucosa may exhibit punctate redness, similar to that of the skin. The tongue is at first furred but later desquamates and assumes a peculiar strawberry appearance, particularly at the border. The eruption at first diffuse and punctiform generally appears on the second day of the disease. The neck and chest are usually involved first although the rash rapidly spreads to other parts of the body. Only the circumoral region is ordinarily exempt. The eruption fully developed at the end of the third or fourth day consists of closely aggregated, pinhead size or larger reddish macules which give to the skin a distinctly scarlet color. Redness disappears on pressure and when the skin is stroked transient white streaks are formed. Petechiae when present indicate grave intoxication, which may be such that death occurs within a few hours after the onset of the disease. In mild and abortive types the eruption may be slight or even lacking. As a rule flaky desquamation commences between the seventh and tenth days and continues for a fortnight. Volar surfaces exfoliate slowly and sheets may come away in the form of casts of the affected parts. Nails are sometimes lost, but hair is seldom shed.



Fig. 189



Fig. 190.

Fig. 189.—Postscarlatinal desquamation. (Drs. Welsh and Schamberg.)
Fig. 190.—Postscarlatinal desquamation. (Dr. H [illegible])

Scarlatiniform eruptions may occur in streptococcic infections of the throat, surgical wounds, burns, or pelvic and postpartum infections. These may be considered true scarlet fever which is simply streptococcic infection with a symptomatic rash. Strains of streptococci differ in erythrogenic power and rashes occurred in from 47 to 0 per cent of those infected with various organisms studied by Hamburger et al (J 124 664 1944). The

Dick test consists in the intradermal injection of toxin lacking antitoxin the susceptible subject responds with erythema while absence of response indicates relative immunity Negative reactors got tonsillitis but no rash, but Dick positives got scarlet fever as reported by Schwentker et al. (AmJHyg 38 27 1943) See Dick and Dick (Scarlet Fever Year Book Pub., 1938)

**Diagnosis.**—In drug rashes the history and the absence of fever angina and other manifestations of infection serve as distinguishing features. Measles is characterized by its longer period of incubation, the primary involvement of the forehead and face, the larger size crescentic arrangement and darker color of its edematous macules, and the catarrhal involvement of the respiratory tract An atropine rash may be accompanied by fever and delirium.

**Treatment.**—Prophylactic doses of toxin given to induce active immunity are likely to be followed by fairly severe reactions which may be avoided by giving 7 graduated doses at weekly intervals (Glazier NEngJM 233 204 1945) Nevertheless persons exposed to the disease occupationally should be protected (Anderson and Reinhardt JInfectDis 517 1936 1935) Convalescent serum given to contacts early seems to abort the disease and even if given later seems to yield symptomatic benefit. Human serum provokes no untoward symptoms.

Sulfonamides given early are quite effective and reduce the incidence of complications. Penicillin is probably even more efficient for no complications occurred in a series of 118 patients so treated by Breese et al (AmJMSc 211 417 1946) High dosage for 8 days is to be preferred and this tends to reduce the carrier rate. Even orally administered 100,000 units q 4 h., it is effective (Hirsh et al J 133 657 1947) Convalescent serum human globulin or antitoxin may do for the severely toxic patient what bactericidal medication alone cannot do Cool moist applications, such as aluminum acetate 1 500, may prove comforting A bland oil is useful during the desquamative stages.

## RECALCITRANT PUSTULAR ERUPTIONS OF THE EXTREMITIES

We follow Andrews (Dis. Skin, Saunders, 1946) in the description of this group which includes forms which have so many characteristics in common that it is difficult to divide them definitely into separate entities. Dermatitis repens, acrodermatitis perstans, and pustular bacterid are practically synonymous.

**Dermatitis Repens (Acrodermatitis Continua)** usually follows an injury small sore or paronychia It is characterized by progressive and rebellious serous undermining of the epidermis with the formation of numerous minute abscesses It begins with localized redness and vesiculation or pustulation. The central portion soon consists of glazed, denuded dermis, and this is surrounded by a ragged border of undermined epidermis. Serum and pus can be squeezed from beneath this marginal collar which ranges from 0 1 to 1 0 cm in width There is little pain or itching. The disease spreads slowly usually remaining unilateral *Staph aureus* generally can be isolated We look upon the disease as a chronic localized form of infection eczematoid dermatitis (q.v.) generally responsive to elimination of foci toxoid immunization and penicillin

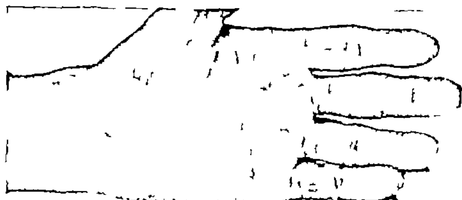


Fig 191

Fig. 192.

Figs 191 and 192—Pustular bacterid (Dr George Andrews)

**Pustular Psoriasis of the Extremities of Barber** (see BJD 54: 72, 91 1942) is generally bilateral and symmetrical, and cultures are usually sterile. Circumscribed lesions of thenar eminences or soles are typical, within which occur crops of minute intraepidermal pustules followed by drying crusting, exfoliation and recurrence. While some of such cases have been cured by elimination of foci, others have proved incurable (Sachs and Scannone JInvD 6 349, 1945) Discussions of the confusing status of various clinically distinguishable manifestations of vesicular and pustular eruptions of the extremities by Dore and by Goldsmith (BJD 54 72, 91, 1942) are interesting. Our present interpretation of these cases invokes infection, secondary infection, focal infection, contactant irritation and food allergy in various combinations and degrees of causative consequentiality (see chronic dermatitis of hands and feet, p 469)

**Pustular Bacterids.**—Andrews et al. (ADS 29 548, 1934) reviewed the features of persistent acrodermatitis, early lesions of which are intraepidermal pustules, which by confluence give rise to visible pustules and by peripheral spread produce crusted patches. They emphasized these uniform features of the varying clinical cases (1) failure of bacteriologic and mycologic examination to reveal organisms (2) unresponsiveness to all forms of local treatment including x ray therapy (3) coexistence of foci of infection (4) therapeutic benefit when these foci are eradicated (5) absence of features of psoriasis, with the pustular variety of which these cases have been confused. Pustular bacterid includes cases in which the only cure rests on removal of foci of infection Foci of particular importance are the teeth, where pyorrhea and decay as well as abscesses are significant, tonsils, sinuses, kidneys, pelvic organs, vagina, and prostate.

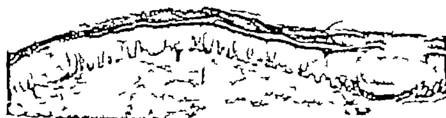


Fig 111.—Pustular bacterid, photomicrograph, showing discrete intraepidermal pustules (Dr George Andrews.)

Paronychial disease of this type is described separately by Andrews. A chronic and recurrently active vesiculopustular dermatitis of the terminal phalanges undermines the nails, deforming them to a greater or less degree. Elimination of foci and contactants, along with penicillin injections, often proves curative.

**Etiology**—Staphylococci and streptococci have both been found Any inflammatory lesion, such as a traumatic one, acts as a filter for whatever circulating organisms may originate from a focal infection (Menkin *Dynamics of Inflammation* Macmillan 1940) See Andrews and Barnes (BMJ 34 1260 1941)

**Diagnosis.**—Infectious eczematoid dermatitis, mycotic infections pustular psoriasis, and primary streptococcic lesions of the extremities must be differentiated. Chronicity and rebelliousness to treatment are typi

features In infectious eczematoid dermatitis the eruption is usually of wide distribution, and the patches are superficial. Fungi are absent.

**Prognosis.**—The disease may persist for months or years. A common sequel is roentgen dermatitis. Response to proper treatment may be gratifying

**Treatment.**—Of local applications moist compresses with 1:10,000 mercuric chloride are commendable Gentian violet or 1 per cent tincture of iodine is a suitable antiseptic. Ointments do not work. One must eradicate foci of infection, eliminate contact irritants, and simultaneously attack with suitable chemotherapy the parasites locally present. When the lower extremity is affected, due attention must be given to circulatory problems, effort being directed at obtaining optimum conditions of blood flow Sulfadiazine by mouth may help greatly (Lever ADS 49 273, 1944) Immunization with bacterial antigens such as staphylococcus toxoid is indicated Penicillin intramuscularly in large doses usually benefits, sometimes cures. X ray therapy must be wisely administered in order to avoid overtreatment.

## LOCAL INFECTIONS WITH GANGRENOUS DERMATITIS

**Hemolytic Streptococcic Gangrene**—Meleney (A Surg 9 317 1924) pointed out that there is usually an initial lesion, which may be an injury or an operative procedure. Alarming rapidity of spread, swelling stiffness, pain fever and prostration characterize the early stages. The skin is first tense smooth, and shiny but soon portions gradually turn darker changing from red to purple then to blue Bullae may form. By the fourth or fifth day the purple areas become frankly gangrenous. A line of demarcation appears, the dead skin separates, and beneath it is revealed extensive necrosis of the subcutaneous tissue Sometimes the area of skin necrosis is small and subcutaneous loss extensive Healing comes about slowly by granulation In severe cases the process continues to advance until several large areas of skin have become gangrenous the patient becomes more intoxicated, metastatic abscesses may develop and death ensues The regional lymphatics are relatively little affected. Blood cultures in many cases show a microaerophilic hemolytic streptococcus, as do cultures from the lesions The synergistic action of streptococci and staphylococci has been indicated by production of the disease in animals.

In treating undermining ulcers, zinc peroxide is recommended. It must be properly prepared to be of service (Meleney and Harvey Ann Surg 110 1067 1939) mixed with equal parts of sterile water and applied everywhere to the surface of the infected tissue The dressing must be a daily one carefully done, for direct and moist contact is essential. Penicillin may halt the progress of the lesion permitting spontaneous separation of the slough and rendering surgical attack unnecessary while sulfonamides, strongly recommended a few years ago have not been wholly successful in controlling the condition according to Meleney et al (Surg 18 423 1945) Many cases of chronic dermatitis with recalcitrant ulceration of the lower leg are due to the streptococcus and respond to full doses of sulfonamides (Taylor J 118 1196 1942)

**Chronic Streptococcic Ulcers** also occur producing cutaneous gangrene which is slowly progressive and resistant to treatment (Goodman J 111 1427, 1938) The undermined borders are irregular firm thickened, ragged and angry red in color The bases are roughly granular

and glazed, discharging a copious serous fluid. Other than light and transient lymphadenitis, there are no complications. A symbiosis of streptococci and staphylococci was postulated as causative of geometric phagedena by Greenbaum (ADS 43 775 1941) See Dostrovsky and Sagher (ADS 54 408 1946) While penicillin by injection is highly effective, the 0.5 per cent wet dressings of cysteine hydrochloride of Hamilton (OklaSMAJ 32 359 1939) deserve mention.

**Gangrenous Balanitis (Phagedenic Balanitis)** is a disease which develops rapidly and may give rise to deep and widespread gangrene. The typical cases are apparently the genital manifestation of Vincent's disease, for the spirochete and fusiform bacillus can be demonstrated, and the response to arsenical medication may be suggestively prompt However synergistic coccic gangrene may affect preputial tissue as well as tissues of the face or legs, the more common location of such lesions Phagedenic ulcers of the genitalia are characterized by extensive and speedy destruction with comparatively little tissue reaction. The slough is greenish gray The odor is putrid and offensive. Fever and intoxication are likely to be great. The regional lymph glands are enlarged and tender Death may result. A copious, purulent hemorrhagic discharge characterized the case of v Haam (AmJTropM 18 595 1938)



Fig 194.



Fig 195.

Fig 194—Gangrenous balanitis (Dr F G. Harris.)
Fig. 195.—Gangrenous balanitis (Dr J H. Moore.)

Necrotic tissues should be cut away in such cases, giving free drainage and access to chemicals Oxidizing agents are used locally hydrogen peroxide potassium permanganate or chlorine water soaks, or the actual injection into the tissues of oxygen gas. Penicillin by injection is of course indicated, and also sulfonamides may be given by mouth.

**Genital Ulceration** in cancer tuberculosis, syphilis, actinomycosis, granuloma inguinale lymphogranuloma inguinale chancroid, paraphimosis, phagedena, gangrenous balanitis ulcus vulvae acutum, and Behcet syndrome require differential diagnostic

consideration (see Carlson: JMoSMA 24 147 1937; Speiser: AmJOG 43: 681, 1943; Leider: USNMBull 41: 278, 1943) Biopsy smear culture, dark field and intradermal and serologic tests are involved.

**Progressive Postoperative Gangrene** is a rare but clinically typical phenomenon of secondary infection of a surgical wound usually abdominal or thoracic. The lesion begins within 2 weeks as an erythematous induration at the edge of the wound. The inflammatory tumor becomes purplish or purpuric, then undergoes central necrosis. Its progress may be extensive, and intoxication, fever and pain feature its course. Streptococci, staphylococci, or both, as well as other organisms, have been found. Treatment comprised radical excision at one time, but one would expect penicillin and antitoxins to accomplish some cures (Touraine and Duperrat: AnndeD 10: 257 1939; Dodd et al. ASurg 42: 988, 1941)

**Massive Destruction of the Face** occurs rarely as a horribly disfiguring and ultimately fatal syndrome which we suspect of being due to necrosis of facial bones from medicinal heavy metals. Dennie and Hamilton (ADS 42: 1040, 1940) attributed their case to pathogenicity of *Spirochaeta microdentium*. The patient of Cole et al. (ADS 43: 943 1941) was a congenital syphilitic.

## SYSTEMIC INFECTIONS WITH GANGRENOUS DERMATITIS

**Pyoderma Gangrenosum** comprises a group of unusual cases characterized by suppurative destruction of the skin associated with infection of long duration elsewhere in the body. Brunsting et al. (ADS 22 655, 1930) described 5 patients, 4 of whom had ulcerative colitis and the fifth thoracic empyema. Skin lesions included blebs, ulcers, pustules, and



Fig. 196.—Pyoderma gangrenosum in typhoid fever (Dr. G. B. Lemmon.)



Fig. 197.—Pyoderma gangrenosum. (Dr. M. C. Stone.)

abscesses, in which *Staphylococcus aureus*, *S. albus* and hemolytic *Str. pyogenes* were found. Ulcers manifest slightly raised, jagged, overhanging and undermined edges and bright red bases dotted with granulations and bathed in foul-smelling yellowish-green pus. They may attain a diameter of several centimeters. The course of the disease is characteristically chronic. Improvement and recrudescence in the internal chronic infectious process are respectively associated with evident

trend toward healing and uncontrollable tendency to spread on the part of the skin lesions. At one time the patient may have scars, pustules, and large integumentary defects, which may be healing or progressing. The total number of ulcers ranges from one to a score or more and response to therapy is erratic. The outcome is doubtful. Some patients have become cachetic and died; a majority, however, have passed through difficult periods with eventual return to health. Much depends on the effectiveness of attempts to correct the underlying condition.

**Treatment.**—Locally one may try Meleney's zinc peroxide paste (Brunsting ADS 41 752, 1940) or sulfanilamide powder (Dostrovsky and Sagher ADS 48 164 1943). Wise (ADS 48 551, 1943) used gramicidin ointment and administered sulfaguanidine, vitamin B complex and vitamin C with benefit. Penicillin should help. Ultraviolet light baths, transfusions, a full diet, acetarsone by mouth and various topical antiseptics have been recommended.

**Gangrenous Dermatitis of Infants (Gangrenous Ecthyma)** is a rare complication of one of the exanthemata. Vesicular lesions becoming pustular develop into oval sloughs, which result in scars if recovery occurs. Trunk, buttocks, and thighs are sites of predilection. A course of weeks or even months is marked by vomiting, chills, fever and intoxication.

**Dermatitis Nodularis Necrotica** is characterized by a recurrent, polymorphous eruption of vesicles, papules, papulonecrotic lesions and ulcers preferring the backs of hands and feet, knees, elbows, and volar skin, with or without constitutional disturbance. Petechiae may occur. Scars and hemosiderin stains result. The hypothesis of tuberculous etiology has been discarded, while that of embolism seems plausible. Bacterial endocarditis brought to autopsy one patient of Duemling (ADS 21; 829 1930; 33; 99, 1936) who found hemolytic streptococci in the skin lesions and lymph nodes of another. Reticulum cell sarcoma produced this picture in the report of Nieman and Wise (ADS 40; 560 1939) but Bernstein (NYSJM 40 737 1940) could not discover the cause in his 3 patients.

## INTERTRIGO

**Symptoms.**—Intertrigo is a superficial dermatitis occurring on apposed surfaces, characterized by redness, maceration and itching. Localized redness, usually accompanied by hyperhidrosis, is the first manifestation. If neglected the skin becomes abraded and raw, often with the formation of vesicles and pustules. The gluteal and cruroscrotal folds, inframammary region and folds of the neck are common locations. In babies, "napkin rash" is the diagnosis often made.

**Etiology.**—Causative factors include friction, warmth, perspiration and excretions supportive of floral growth. The usual offenders include the staphylococcus, streptococcus, monilia, and mycelial fungi singly or in combination. The disease is especially common in obese persons, and during the hot months. Leucorrhea, urine, and other discharges may be instrumental in its production, and diabetic subjects are particularly prone to attack. Irritation of the skin by clothing, soap or hard water may render it vulnerable. Compare streptococcic dermatoses (p. 174) and moniliasis (p. 328).

**Treatment.**—In addition to keeping the parts clean, the liberal use of a powder such as zinc stearate or a mixture of zinc oxide and starch is advisable. Ointments do not act well in these cases. Gentle sponging with a cool nonirritating antiseptic, such as 1:10,000 bichloride of mercury or 1:5,000 $KMnO_4$ is beneficial. The parts are dried by tapping with a soft towel and a bland powder is freely applied. Sulfo-

powder has been recommended Occasionally it is necessary to separate the affected parts by means of supportive brassiere or powdered pads. If there is oozing the areas may be painted with 2 per cent aqueous gentian violet Good ventilation, even an electric fan and drying radiant heat may be utilized, along with aluminum acetate baths, half an ounce to 10 gallons of cool water

**Napkin rash** has been attributed to ammoniacal decomposition of urine and boric acid powder and boric acid rinses of diapers may be tried. Since the diagnosis of napkin rash is about as explicit as that of athlete's foot, critical investigation of etiologic factors such as soap baby oil, antiseptic diaper rinses and other contactants or scabies, or infectious impetiginoid disease, or moniliasis should be made, following which, efficient treatment may be designed. (See Gordon BMJ 1 383, 1940 Forman Pract 146 238 1941 )

## ERYSIPELOID

Erysipeloid is the infection caused by *Erysipelothrix rhusiopathiae* the bacillus of swine erysipelas, which generally reaches the human host through contact with a infected animal cadaver infecting not only butchers but also veterinarian students (Gross JKansMS 41 329, 1940) This fine, rod-shaped, nonmotile, gram positive organism can be cultivated from the deep tissues of infected skin (Watt JPathBact 50 355 1940) It may be seen in Gram-stained sections in the deep capillaries of the

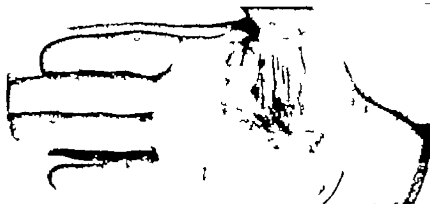


Fig. 188 —Erysipeloid, palmar lesion of 3 days' duration in a battoir employee following puncture wound by a hog bone. (Klauder J 111 1345, 1938.)

dermis accompanied by inflammation ranging from serous and edematous to leucocytic with or without suppuration, noted Klauder (ADH 50 151 1944) who described the diamond skin disease in hogs and discussed in human beings 3 forms (1) localized, occurring at the site of occupational inoculation exhibiting limited spread, central clearing, and the formation of marginate figures rarely vesicular, often accompanied by periostitis and arthritis (2) diffuse and generalized exhibiting sharply marginated extending lesions which heal [illegible] older regions, repeated relapses, but few or no subjective symptoms and (3) septicemic exhibiting septic fever sometimes endocarditis (Russell and Lamb J 114 1045 1940) with or without cutaneous manifestations which may comprise plaques, unusual lines purpuric lesions located at creases and on palms and soles, or hematoma like swellings of the ears. Prolonged arthritis is a common sequel often affecting wrists, elbows and shoulders.

**Treatment.**—Sulfathiazole in less than [illegible] application relieves pain promptly It rarely required more than 3 times in 3 to 6 days [illegible] cures localized infections in a week or so as a rule according to Griswold and Howen (ADH 49: 245,

1944) Sulfonamides have been used with fairly reliable success (Sehorh and Shelmire: ADR 41: 570 1940) Immune serum may be preferable to sulfonamides, and both may be given in resistant cases, stated Klauder and Rule (ADR 40 27 1944) The organism was shown to be penicillin sensitive by Hellman and Herrell (PSMMC 19 140 1944), and prompt and excellent results with penicillin by injection have been reported (Costello: ADR 52: 400 194 ; Hodgson BMJ 1: 463 1945; Ehrlich AIntM 78: 565 1946 Klauder and Rule JInvD 329 1946) Streptomycin is not effective.

## GONORRHEAL DERMATOSES

Gonorrheal dermatoses are cutaneous manifestations of gonorrheal infection, either direct or metastatic

**Exanthemas** in acute gonorrhea include erythematous, papular and scarlatiniform rashes, and rarely purpura. Annular erythema complicated a case of vulvovaginitis. Purpura and bullae with arthritis and a positive blood culture have been reported. (Keil QJM 7 1, 1938 )

**Skin Lesions** of primary gonococcal infection have been classed as (1) folliculitis, (2) ulcer, a simple or serpiginous blenorrhagic chancre, (3) abscess, and (4) circinate balanitis, by Kroll et al. (AmJS 28 320 1944) whose cases included a fluctuant abscess containing chocolate colored pus on the shaft of the penis, a pustular bleb near the frenum and a painless subcutaneous abscess in the foreskin. Furunculoid lesions have been noted (Lowry and Franks AmJS 27 428, 1943) A pustule with lymphangitis developed in a laboratory worker accidentally inoculated with a pure culture (Seus AmJS 31 60 1947)

**Keratosis Blennorrhagica** is a chronic inflammatory dermatosis, occurring in conjunction with gonorrheal infection of the genital tract and of the joints, characterized by a symmetric eruption of horny conical nodules, pustules, and crusts on the palms and soles and other parts of the body It is practically invariably associated with multiple arthritic involvement. The onset follows specific urethritis by several weeks or months. The disease is rare

Keratosis blennorrhagica is evidence of grave systemic disease, stated Lalany and Hughes (ADR 54 150 1946) in a review of 163 cases. Its manifestations are preceded by several days, weeks, or months by gonorrheal urethritis, prostatic and seminal vesicle infection being often present too. Arthritis nearly always appears before skin lesions do. The exanthem is of sudden onset, associated with chills and fever Its distribution is symmetric, with predilection for feet soles, ankles and hands, and it appears also about the arthritic joints and the genitals. It may be widely disseminated or localized to the extremities. Typical lesions start as pinhead size or slightly larger vesicles firm, surrounded by erythema, becoming pustular with dry caseous contents. These ulcerate and develop dirty hard brown crusts with firm horny collars. Hemorrhagic blisters and erythematous patches may often be found in addition. In later stages there is extensive coalescence of mature lesions forming relief maplike areas perhaps affecting an entire sole palm, or joint region. Such confluent areas have a dusky red slightly moist base and sharp slightly raised margins, and are covered with dry powdery scales perhaps resembling psoriasis Toes and fingers show diffuse slightly moist erythematous involvement of the terminal phalanges on which the tense vesicles are scattered but these do not enlarge or pustulate. This may resemble acrodermatitis perstans. Nails become dry and brittle and may be lifted from their bed by heaping up of subjacent horny material. The disease prefers men in the fourth decade who have had gonorrheal urethritis repeatedly Mortality has approximated 10 per cent Neisserian organisms have been demonstrated in perhaps 1 per cent of the cases

**Etiology**—Barrett (ADR 22 62 1930) recorded cases of keratoderma, in one of which the gonococcus was found in the vesicles, pustules, and abscesses, but such search has proved fruitless in the experience of many others Gonorrhea is always present elsewhere, however



Fig. 199.—Gonorrheal abscess on shaft of penis. (Sobel ADS 45 622, 1942.)

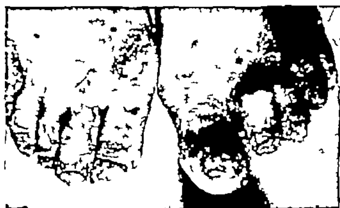


Fig. 200.—Gonorrheic keratoses. (Keim ADS 9 422, 1924.)

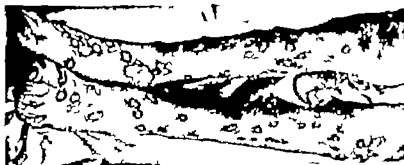


Fig. 201.—Gonorrheal keratoderma. (Haase JCutD 34 317 1916.)

**Diagnosis.**—Pustular and arthropathic psoriasis are distinct entities (Epstein: ADS 40 547 1939; BJD 51: 425, 1939) Reiter's syndrome (see following) is to be distinguished, but Lodany and Hughes believed some of these to be gonorrheal.

**Treatment.**—Elastoplast occlusive dressings and fever therapy were recommended by Taylor (BJD 51 418, 1939) Hyperpyrexia has been accepted as effective since the report of Epstein (AmJS [illegible]: 148, 1937) Penicillin alone is sometimes curative (Emmet: ADS 53 378 1946) but failure has been experienced. Streptomycin was reported extremely effective, a single injection of 0.5 gm. or more being curative (Cahn et al.: AMJS 31: 265 1947) Combe and Behrman (ADS 46 728, 1942) gave massive doses of vitamin A and penicillin. Skin lesions cannot be eradicated until foci are successfully eliminated. Locally an ointment containing resorcinol and sulfur may help and x ray therapy has been advocated.

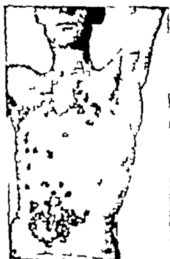


Fig. 191.



Fig. 192.

Fig. 191.—Gonorrheic keratosis. (Dr Marcus Haase.)
Fig. 192.—Gonorrheic keratosis. (Epstein AmJS 21 148, 1932.)

**Reiter's Syndrome** comprises a triad of arthritis, conjunctivitis and urethritis not caused by known micro organisms (Lever and Crawford ADS 49 389, 1944) It may exist when the triad is incomplete according to Hollander et al. (J 129: 593, 1945) Young males are affected, and arthritis, usually multiple dominates the picture. When arthritis with exacerbations, has existed for one or a few months, urethritis and conjunctivitis appear These usually subside after a few weeks. Cutaneous lesions resembling those of keratosis blennorrhagica have occurred in some cases. Gonorrhea, however cannot be found, and despite the purulence of the disease sulfonamides and penicillin do not influence it. The affected joints are red, hot, swollen, and tender but the condition is self limited generally clearing within 6 months. It is not rare according to Finck (AmJMSc 214 76, 1947) Recurrences may take place Patients suffering from apparently this syndrome have been reported with bacillary dysentery (Herson; Marsh BMJ 2 875, 1946) A virus was isolated in a case of Dunham et al. (JUrol 58 812, 1947) Treatment is symptomatic Mapharsen helped cases of Khoury (JUrol 58: 265 1947)

**Behcet's Syndrome** comprises a triad of genital ulceration, oral aphthae, and uveitis or iridocyclitis in repeated attacks which, in later stages, is associated with hypopyon (Berlin: ADS 49 227 1944) Curth (ADS 54 179 1946) recognized formes frustes in which only genital or oral or eye lesions may occur Ulcus vulvae acutum may be a manifestation, even including the finding of B crassus. Ocular symptoms may precede or follow other features of the triad; both eyes are eventually involved, and blindness is likely to result Retinal and vitreous hemorrhages may occur (Katzenellenbogen: BJD 58 161, 1946) Cutaneous lesions appear in some

cases including erythema nodosum and erythema multiforme-like acneic and papulo-pustular eruptions. The skin is markedly sensitive, so that trauma provokes pustules, and erythema follows any injection.

The cause is not known, but Behcet (Bécfrane D 46 674 1939) suspected a virus. Histologic examination has revealed nothing specific. Treatment has been disappointing but focal infection should be eliminated, and sulfonamides, penicillin, transfusions and smallpox vaccination may yield benefit.

## MENINGOCOCCIC DERMATOSES

**Symptoms.**—*Neisseria intracellularis* (meningococcus) is the infectious agent of epidemic meningitis, which, particularly in certain epidemics, is associated with petechial and purpuric lesions. If such lesions are pinched, pricked and squeezed, and the droplet of blood and tissue juice



Fig. 201.



Fig. 203

Figs. 201 and 203.—Rashes of meningococcemia. (Mitchell Heggs, BJD 54 283, 1942.)

is prepared with Giemsa, Wright or Gram stain, the diplococci may be found in perhaps 80 per cent of the cases (Tompkins J 123 31 1943). Conjunctival exudate, herpetic fluid, and the urine may likewise yield meningococci for early diagnosis (Sophian J 125 376 1944).

Herpes simplex, commonly of considerable severity, accompanies meningococcal infection frequently. Toxic erythema and rheumatism may be seen, and serum sickness and dermatitis medicamentosa may appear in the meningitic patient. Acute catarrhal conjunctivitis often accompanies the infection and may comprise its sole manifestation (Theodore and Kost AOphth 31 43 1944).

With regard to rashes in the acute disease, distinctive is an irregularly round hemorrhage with a gunmetal-colored center composed of pus cells (Appelbaum: (AmJMSc 193 96, 1937) The types of eruption emphasized by Costello (J 134 518, 1947) were (1) those resembling erythema nodosum, (2) petechial puncta interspersed with large hemorrhagic blotches, (3) lesions resembling flea bites with central hemorrhagic punctum and faint erythematous areola, and (4) necrotic depressed lesions more or less simulating the papulonecrotic tuberculid. The earliest lesions are ill defined erythematous macules in a dependent location by predilection, and the rash is multiform, variable yet characteristic (Hill and Kinney: J 134 513 194 ) Petechiae favor the joint regions and pressure areas. The face palms, and soles are rarely affected. Lesions usually appear within 1 to 36 hours after the onset of disease and they may fade in a few days irrespective of therapy See purpura symptomatic, and the adrenal hemorrhage syndrome

Chronic Meningococcemia occurs sometimes without meningitis. It may begin suddenly with fever pai in the joints, chilly sensations, and skin lesions. Suppurative arthritis is not found but arthralgia is without eff ion. Cutaneous manifestations appear in the first week and crops come out with each rise in temperature, the lesion being various. A characteristic form is a rose-colored macule with a central vesicular pustular or petechial element (Ochs et al.: BullUSAMD Sept., 1944), or small, faint red macules or papules resembling erythema nodosum, or petechiae of small o considerable size may be seen. An apparently insignificant rash i diagnostically as important as purpura, stated Hill and Lever (J 1.3 9 1943) Tender pea sized, erythematous nodules appearing in crops were reported by Ingram (BJD 54: 228 1942) in patients with positi blood culture es. In addition to macules papules, vesicles, and petechiae, Mitchell Heggs (BJD 51 43 1942) described ulcers, sloughs, and dermatomyositis.

**Treatment.**—Sulfonamides internally perhaps given intravenously at first are extremely efficient. The organism is also sensitive to penicillin.

## TULAREMIA

**Symptoms.**—Tularemia is the disease caused by *Pasteurella tularensis* which commonly infects rabbits, from which it is conveyed to man by inoculation usually at the site of a minor abrasion.

Many vectors are recognized the vertebrates being listed by Burroughs et al. (JInfectDis 76 115 1945) while insects are occasionally and ticks are often carriers (see PH Rpt 55 667 1940) The organism may be transmitted from animal to animal and from animal to man by wood ticks (epidemic reported by Byfield et al. J 121: 101 1943) dog ticks, and deer flies The pelts f infected animal also convey the infection. About 3 to 4 days after exposure illness begins suddenly with headache chilliness, vomiting, fever prostration and aching pai all over the body Such symptoms are readily mistaken for influenza. The tularemic chancre when present usually occurs on the hand and develops slowly as a painful papule which soon sloughs, forming a soft flabby painful, punched-out ulcer Regional lymph nodes enlarge first becoming painful tender and centrally necrotic sometimes suppurating through the skin. Lymphadenitis may become general. Illness and fever persist perhaps f r 3 weeks, but convalescence is low and is characterized by great weakness and disability which may continue for several months. Most patients recover fully but mortality ranges about 5 per cent the development of pneumonia being common Hunters, vendors butchers, and housewives re especially exposed. Laboratory personnel working with the organism rarely escape A wild rabbit should never be handled with the bare hands. Infected meat is rendered saf by thorough cooking.

The ulceroglandular type i more common, but a primary sore is not always present. In it absence the case is classed a typhoidal T laremic pneumonia may develop in either Of 223 cases, among which occurred 17 deaths, 181 were ulceroglandular 7 were oculoglandular (the chancre being about the eye) 14 were typhoidal and 23 simply glandular (Pullen and Stuart 129 495 1945) The hands and fingers bore the primary sore in 1 5 cases Subcutaneous lymphangitic nodules were present in 19 cases, and these were firm, movable nontender as a rule but ttached t the skin and ulcerative in few instances Erythema nodosum-like les ons were found in 6 cases. A diffuse papular rash occurred in 9 cases ppearing usually in the second or third week, lasting usually only a few da s. It was prominent on arms and neck, was bilateral and symmetric and included erythematous macules on the palms. Of the deaths 1. were due t pneumonia nd 1 to tularemic meningitis. Hitch and Smith

(ADS 38: 850 1938) described tularemic eruptions, noting the primary ulceration, which may be mucosal and the generalized rashes, in which macules, papules, vesicles, and pustules have all been recorded.

**Diagnosis.**—Tularemia must be differentiated from typhoid fever, glanders, anthrax, actinomycosis, and sporotrichosis. Significantly high or rising titer of the agglutination test is diagnostic (Simpson: OhioSMJ 29 35, 1933) Positive blood cultures and animal inoculations of aspirated material may also be used in identification. *Antigen for a skin test was made from necrotic lymph node material by Lavies* (ADS 44: 147 1941) The skin test seemed highly specific during the first week, perhaps before the agglutination test becomes positive (Friedewald AmJMSc 197 493, 1939) The opsonocytophagic reaction parallels the agglutination test, and may help to distinguish brucellosis, which cross agglutinates with tularemia.



Fig. 206.—Tularemic chancre 18 days after its onset in a market man who dressed rabbits (Brown and Hunte in Stitt' *Diagnosis and Treatment f Tropical Diseases*, Blakiston's)



Fig 207



Fig 208.

Fig 207.—Tularemic lymphadenitis. (Dr Walter M. Simpson.)
Fig. 208.—Acneform ruption in tularemia. (Dr Walter M. Simpson.)

**Treatment.**—Strict bed rest is indicated. Surgical interference is useless and even dangerous. *X ray therapy relieves pain of local lesions. Streptomycin* was found effective in the disease under experimental conditions by Heilman (PSMMO 19: 553, 1944) and its superiority to specific antiserum was recognized by Foshay and Pasternack (J 130 393 1946) and Foshay (JIndianaMA 41 207 1948). Streptomycin, 7,000,000 units in 10 days, cured a pneumonic patient in whom penicillin and sulfonamides had proved ineffective (Cohen and Lasser J 131 1126, 1946) although sulfonamides have been reported helpful in the past. We have seen Foshay's antiserum (YBPath 1940 p. 445) yield excellent results. If streptomycin were unavailable, one might use this serum with neoarsphenamine as recommended by Werling (OklaCMAJ 35: 103 1942) or per cent sodium bismuth tartrate 1 c.c. per 100 pounds daily, intravenously as reported favorably in 61 cases by Jackson (AmJMSc 200: 513, 1940)

## GLANDERS

**Symptoms.**—Glanders is due to *Malleomyces mallei*. The infection, acute or chronic, is characterized by the occurrence of vesicular pustular, and ulcerative lesions, along with systemic symptoms. It is a comparatively common disease of horses, mules, and donkeys, but it is fortunately a rare disease in man. The early symptoms are those of mild septicemia: malaise, vague joint pains, fever of intermittent type and prostration. Profuse catarrhal or purulent nasal discharge is regularly present, particularly in acute cases.

*In the acute form the manifestations of systemic involvement gradually become* more marked, and the patient sinks into a typhoidal state, and generally dies. The cutaneous symptoms are varied. In cases in which infection has occurred through the skin, the initial lesion may be carbuncular papular or vesicular. More or less induration is present, however and superficial sloughing is common. Characteristic lesions develop in 1 to 4 weeks, as groups of small, deep-seated reddish or yellowish papules, which sometimes become vesicular or bullous, but which invariably sooner or later form ulcers. These may coalesce giving rise to large, gangrenous areas. Lymph node involvement results in the formation of subcutaneous nodules, farcy buds. These tumors are likely to perforate the overlying skin, giving rise to foul, suppurating ulcers.

In the chronic form the lesions are fewer in number and less violent in character. Catarrhal symptoms develop late, if at all. The disease may persist for months or years. Abscesses and ulcers are occasionally associated with metastatic foci in subcutaneous and muscular tissues, joints, and lungs.

Glanders occurs mainly in men whose occupations bring them in contact with horses. The organism is highly pathogenic, and has caused the death of many laboratory workers. Strict isolation is required. Six cases occurring in laboratory research workers were recorded by Howe and Miller (AnnIntM 26: 93 1947) 5 of whom were infected via the respiratory tract as judged by the presence of pulmonary lesions.

**Diagnosis.**—The involvement of the nasal mucosa is the most characteristic feature. This, the skin and lymphatic involvement, and the usually typhoid like constitutional symptoms should prevent confusion. Intradermal and complement fixation tests are available.

**Prognosis.**—Practically all cases have terminated fatally

**Treatment.**—Mallein, an endotoxin which corresponds with vaccine has been tried with some degree of success. In addition, surgical measures are to be employed. Serum and vaccine therapy are not satisfactory Sulfadiazine may be recommended (Howe and Miller: AnnIntM 26 93 1947)

## MELIOIDOSIS

Melioidosis is a glanders like disease which occurs primarily in rodents and also in man, Stanton and Fletcher (Studies Inst. M. Res. F M. S., 21 1932) having collected 83 cases of human infection with the *Pfeifferella whitmori (Ac t i nobacillus pseudomallei)* Abscesses, pustules, and sinuses are found, although the important lesions are consolidations and abscesses of the lungs, liver spleen, sometimes the kidneys. This septicemia in man usually is fatal within 3 or 4 weeks. Acute and chronic forms are seen. In the acute, cholera like vomiting, collapse, purging, and death may occur in 7" hours. In chronic forms, multiple abscesses may develop in all organs except the brain, particularly affecting the lungs, spleen and liver Cutaneous vesicles and pustules may simulate variola. The essential pathologic lesion is a small area of necrosis developing into an abscess, coalescing with near by lesions of similar character, and forming a honeycomb containing creamy or in the liver glairy greenish pus (Edit. BMJ 1 344, 1947) A chronic case from the Western hemisphere was reported by McDowell and Varney (J 134 361 1947) and sulfonamides, penicillin, and streptomycin were ineffectual wide cautery excision helped most.

## BRUCELLOSIS

**Brucellosis.**—Three types of organisms belong to the Brucella group *Br melitensis*, associated with undulant fever; *B abortus*, more virulent for human beings than the others, and *B suis*, which is perhaps the commonest cause of human brucellosis. A *typhoid like roseola* appears in about 5 per cent of the cases. An ulcer localized on the face and a case resembling dermatitis herpetiformis have been described.

**Skin Test.**—Culture filtrate may be given intradermally as a diagnostic test. The reaction usually appears promptly showing wide erythema and central edema, which may even slough, along with constitutional symptoms. Reaction may be delayed

(Flannery J 114: 1-84 1940) The test or repetitions of it may be alone of considerable therapeutic value The test is negative unless the reaction persists for 7 to 10 days it may persist much longer While the test depends on tissue sensitivity induced by the presence in the body of organisms of the Brucella group, it i invalid unless supported by active symptoms of the disease (Ervin and Hunt J 109: 1966, 1937)

Brucella Dermatitis.—Of 50 practicing veterinarians subjected to inquiry by Huddleson and Johnson (J 94: 1905, 1930) 60 per cent admitted developing a rash on the arm when it was inserted into the vagina of cows which in their opinion were infected with *Br abortus*. The manifestation of eczematous reactivity makes it appearance in 20 minutes, and depending on the degree of sensitivity, it is (1) light red and blotchy or red and uniform, and itchy or burning but not edematous, persisting for 4 to 8 hours and disappearing without desquamation; or it is (2) papular the lesion being discrete and elevated, not highly pruritic, lasting 3 or 4 days and changing to a brown color before disappearing without exudation or desquamation.

## CHANCROID

**Symptoms.**—Chancroid or soft chancre is due to inoculation, usually venereal with *Hemophilus ducreyi* which soon produces small autoinoculable, painful ulcers of relatively benign character usually located about the genitalia The earliest manifestation a minute reddish macule appears at the site of inoculation after an incubation period of 3 to 14 days. It quickly becomes an inflammatory pustule which ruptures and forms a small shallow circumscribed ulcer The ulcerative lesions may become single through confluence of multiple early lesions, although they may remain multiple As a rule they are circular or oval with soft non-indurated, slightly undermined edges, and grayish granular floors bathed in pus. A reddened areola is usually present although there is but little induration except in chronic lesions. Chancroidal ulcers, being autoinoculable spread by expansion, inoculation, and coalescence. The duration ranges from 10 days to several months. Giant and destructive ulcerative lesions are occasionally seen Extragenital sores are seen but are rarely primary

The regional inguinal lymph nodes are infected, and the bubo may suppurate This involvement may be unilateral or bilateral. It is accompanied by pain and fever (Sullivan AmJS 24 482, 1940 monographic)

**Etiology**—*H ducreyi* is a small slender nonmotile nonspore-bearing, non-acid fast gram negative bacillus, which generally forms chains. It can be grown with difficulty but the technic of Beeson and Heyman (AmJS 29 633 1945) enabled them to obtain diagnosis by cultures in three-fourths of their cases. There is evidence that the bacillus of chancroid sometimes exists in the female genital tract as a saprophyte In smears from the ulcer the organisms may be found as small ovoid rods arranged in pairs, groups or chains lying parallel to one another They may be intracellular or extracellular

**Pathology**—Superficial necrosis pervaded with polymorphonuclear leucocytes, and a peripheral zone rich in plasma cells, lymphocytes, and perithelial and endothelial leucocytes characterize the lesion.

**Diagnosis.**—In syphilitic chancre the period of incubation is long from 2 to 6 weeks the lesion is comparatively painless erosion but not ulceration is typical lymph node involvement is characteristic, the nodes being firmly elastic nutlike painless, and freely movable and *Spirochaeta pallida* can usually be found in the lesion Mucous patches of the genitalia are always accompanied by other evidence of syphilis. Cancer usually

develops after the fourth decade of life chancroids before that period In cancer there is often a history of long continued irritation and the lesions develop slowly and are always indurated

MIXED INFECTIONS.—In lesions due to the conjoint presence of syphilis and chancroid, prolonged observation is required to exclude syphilitic infection. Dark-field examinations help. These should be performed on several successive days during which treatment is limited to saline dressings. Serologic tests for syphilis should be made monthly for 6 months (see J 116 2405 1941)





Fig. 209 Fig. 210

Fig. 209 —Chancroid.
Fig. 210 —Penile chancroid and digit l autoinoc lation. (Dr O (L Coat )





Fig. 211 Fig. 212

Fig. 211 —Chronic [illegible] (Dr H. K. Cole)
Fig. 212 —Ch[illegible] (Dr H. K. [illegible])

SKIN TEST The vacc[illegible] may be used by intradermal injection as a specific diagnostic test [illegible] (Saunders et al NYSJM 39 44, 1939 [illegible] (J 10 [illegible] 1934) found that sterile pus from the chancr[illegible] will serve in lieu of vaccine. There [illegible] an interval of at [illegible] from the appearance of the sore until the

development of demonstrable skin allergy to the specific antigen. Sensitization does not develop unless considerable regional lymphadenitis occurs (Dienst and Gilkerson AmJS 31 65 1947) A positive skin test may be obtained even 30 years after infection. Positive reaction only means a past or present infection.

Biopsy yields specific diagnosis in some 90 per cent of cases, cultures in 75 per cent, smears in only 50 per cent, according to Heyman et al. (J 129 835 1945) The skin test alone is inadequate. Diagnosis by autoinoculation may be considered (Strakosch et al. JInvD 6 95 1945)

**Prophylaxis**.—A 10 per cent aqueous solution of Zephiran chloride and a 2 per cent solution in propylene glycol were 100 per cent effective in preventing experimental inoculations if applied within one hour (Combs and Canizares ADS 51 237,1945) while mild mercurous chloride and 15 per cent sulfathiazole emulsion were 85 per cent effective if applied within 6 hours. Soap alone was not effective.

**Prognosis.**—Chancroids heal readily as a rule. Occasionally ulceration is extensive Complication with phagedenic coccle or Vincent's infection may lead to serious fulminating destruction. If the ulcer is excised or is adequately drained by circumcision before the bubo has developed, the bubo fails to develop

**Treatment.**—Cleanliness is the first requisite. Violent chemical measures are more frequently harmful than beneficial, although cauterization with nitric acid was a time-honored procedure. Phimosis complicating mild astringent applications, such as 1 500 aqueous solution of aluminum acetate may be employed until the inflamma ion subsides. Circumcision diminished the average period of hospitalizat n by 4 days (Rauschkolb ADS 39 319 1939) A popular pre-sulfonamide method of management consisted in moist antiseptic soaks alternated with drying in air under the influence of radiant heat and a dusting powder such as iodoform. Beneficial soaks are hydrogen peroxide, warm 1 5 000 potassium permanganate and 1 10 000 bichloride of mercury Foreign protein therapy occasionally proves helpful. Specific vaccine treatment has been especially successful in chronic serpiginous ulcers. Injections are given intravenously at intervals of 3 days. The dose must be conservative, and fever may be expected.

Sulfanilamide yields remarkably beneficial effects (Kornblith et al. NYSJM 39 364 1939) a dose of 1 gm. each 6 hours being recommended In the absence of bubo 21 gm of sulfathiazole in 5 days cures as efficiently as larger doses, while in the presence of bubo 7 days of treatment do as well as 14 and experimental infections are cured in 3 days, according to Combs et al. (AmJS 27 700 1943) Sulfonamides will not cure all phagedenic cases (Canizares and Cohen ADS 42 649 1940) Sulfanilamide powder may be applied locally and it may be packed into an abscessed bubo when this is opened. The bubo if fluctuant, should be punctured, pushing the knife through normal tissue at the periphery The content is expressed, antiseptic injected, and a pressure bandage applied. Penicillin is without value in chancroidal infection (Pereyra and Landy USNMBull 43 159, 1944) despite the fact that the organism is susceptible to penicillin in vitro (Tung and Frazier AmJS 29 629 1945) Uncomplicated cases respond to bed rest and *sulfathiazole 21 gm. in 5 days if simple, 29 gm. in 7 days* if bubo is present, the drug being given 2 gm. to start with and 1 gm. four times a day (Combes NYSJM 40 1700 1940) More is not necessary

Streptomycin cures chancroidal infection in rabbits (Mortara et al AmJS 81 20, 1947) and 15 human cases, proved by culture, were cured by streptomycin by Hirsch and Taggart (JVDI 29 47 1948) Jawetz (ADS 57 916 1948) cured 15 cases with 10 gm. given in 5 days.

## ULCUS VULVAE ACUTUM

**Symptoms.**—The disease apparently an entity occurs in the form of vulvar ulcers in girls not exposed to venereal infection. Half the patients were virgins in the 20 cases of Olson (ADS 1 279 1920) Finnerud (ADS 13 55, 1926) described the two types, gangrenous or severe, and veneroid, which is more common. See Behcet's Syndrome (p. 189) and compare Vesicular Stomatitis (p. 133)

GANGRENOUS.—The lesions are multiple but few in number located usually on contiguous aspects of the labia minora, accompanied by redness, swelling, and burning pain. The onset is sudden, with fever as high as 40 C. The lesions are pea to dime size, round, with reddish areolae. The edges are soft and steep. The membrane covering the surface is thick or thin, gray yellow or bluish black, and firmly adherent to the base It separates in 3 to 4 days, exposing the soft ulcer which has a smooth floor with a thin fibrinopurulent coating. Fever and pain disappear at this time, and healing is complete in 20 days or so. A sharply circumscribed smooth, atrophic scar results.

VENEROID.—This resembles chancroid but Ducrey's bacillus is not present. Symptoms are mild. The tender ulcers are shallow and are located usually at the introitus. They vary in number and size. The edge is serrated and the shape rounded oval, irregular or fissure-like. New ones appear as old ones heal so that the disease last a month or more. On the labia majora there may occur a miliary eruption of pinhead size lesions, with slightly elevated margins and depressed purulent centers, which persist only a few days. Smears reveal multitudes of *Bacillus crassus*, which closely resembles nonpathogenic *Lactobacillus acidophilus*. Virgins are the victims in 70 per cent of the cases. Papuloerythematous or vesicular rashes, sometimes pustular of general distribution rarely accompany the disease

**Etiology.**—Factors capable of lowering the patient's local tissue resistance hypothetically render the saprophytic *B crassus* pathogenic. The organism is identical with Doderlein's vaginal bacillus and is ever-present in the leucona, existing as a thick (0.5 micron) and usually long (3 to 9 microns) gram positive bacillus with end sharply right angled to its long axis It is easily demonstrated in smear preparations from the ulcer surface. Compare vulvovaginal herpes simplex.

**Treatment.**—Weak antiseptics and rest suffice. No specific agent is known, but the disease is benign and apparently self limited

## GRANULOMA PYOGENICUM

**Symptoms.**—Granuloma pyogenicum is a small pedunculated angiomatoid granuloma, thought to result from infection with *Staphylococcus pyogenes* The lesions are pinhead to cherry size, rounded, reddish pedunculated, mushroom like tumors. They bleed on slight provocation They usually spring up at the site of some slight abrasion or at the margin of a wound. They are generally painless but tender Parts exposed to trauma the hands and feet are sites of predilection. Granuloma pyogenicum of the gum has been called epulis granulomatosa The tumors develop quickly and after attaining their full size persist for weeks or months unchanged. If clipped off, they promptly recur This tendency to relapse has caused granuloma pyogenicum to be mistaken for sarcoma Sometimes a lesion possesses an epidermal covering and so is dry lavender and opalescent, granuloma telangiectaticum These are usually sessile and are brownish and sometimes scaly (Wile JCutDis 28 662, 1910 Sutton J 66 1613 1916 Kelly ADS 31 864, 1935)

The lesions seem to bear the same relation to granulation tissue that keloid bears to cicatrix (Berger et al APath 21 273 1936) and they are not related to botryomycosis.



Figs. 213-215. Fig. 216.

Figs. 213-215.—Granuloma pyogenicum, finger-tip and lip cases.
Fig. 216.—Granuloma pyogenicum of left thenar skin.



Fig. 217.—Granuloma pyogenicum, showing histologic resemblance to hemangioma.





Figs. 218 and 219.—Granuloma pyogenicum of tooth socket and of tongue. (Dr. Howard Fox.)

**Etiology and Pathology.**—The disorder is similar to granulation tissue or proud flesh. *Staphylococcus pyogenes* has been recovered from the lesions. Since new lesions do not develop by reinoculation local changes are probably also essential. The tumors are composed of newly formed vascular tissue so permeated with blood vessels as to resemble hemangioma. There is widespread infiltration mainly of connective-tissue cells with a few leucocytes intermixed, round cells, plasma cells, and mast cells. Clumps of staphylococci are scattered through the growth. Cross section of a lesion widely excised shows its bulging elastic, translucent, whitish composition arranged as a cone-shaped mass lying within the skin, the apex at least as deep as the level of the sweat glands; this explains the failure of clipping off at skin level as a method of treatment.

**Treatment.**—The lesions are harmless but persistent. Excision followed by cauterization is successful if adequately destructive. Radiotherapy can be used (Elsen, Canad.M.A.J. 42: 528, 1940).

**Staphylococcic Actinophytosis (Botryomycosis)** is a rarely recognized entity distinct from granuloma pyogenicum (Berger et al., [illegible] Path. [illegible], 1936). The lesion is a small tumor containing a granular sanguinopurulent exudate within which are microscopic granules simulating those of actinomycosis. Crushed or cultured, these bodies are found to be composed of masses of nonhemolytic but coagulase-positive *Staph. aureus* (Drake et al., J. 123: 339, 1943). In at least [illegible] of the reported cases foreign bodies have been discovered in the lesions.

## VERRUGA PERUANA

**Synonyms.**—Peruvian warts, Oroya fever, Carrión's disease.

**Symptoms.**—Verruga peruana is a disease endemic within certain inland portions of Peru, due to infection with the *Bartonella bacilliformis*. It is characterized by fever of an intermittent, remittent, or irregular type, followed or accompanied by rapid and progressive anemia and the eruption of pinhead to pea size red wart-like inflammatory tumors. The disease is limited in its geographical distribution to the region between latitudes 8 and 13 S. in Peru, between altitudes of 2,800 and 9,000 ft. on the west slope of the Andes. It is especially likely to be contracted in hot ravines which are sheltered from high wind (Fox, J. 104: 953, 1935). Lactescent plants and the insects on them are involved in its transmission.

*Benign* and *malignant forms* of the disease are seen, the malignant variety being severe, acute, and productive of profound anemia.

The period of incubation ranges from [illegible] to 6 weeks or longer and is characterized by fever of irregular type, joint pain, headache and backache, and anemia of severe grade. On the appearance of the eruption these symptoms gradually subside and may disappear. Early cutaneous manifestations are usually purely erythematous. The distribution is roughly symmetric and more or less general, although the face, neck, and extensor surfaces of the arms and legs are the sites of predilection. The mucous membranes are early involved. Within a few hours or days, groups of papules, many of which later become nodules, develop in the erythematous spots. These lesions are of various sizes, from 0.3 to 2.0 cm. in diameter, bright or dark red in color, and sensitive to touch. They may be sessile, cylindric or pedunculated. Their capsules are thin and fragile and readily rupture, giving rise to hemorrhages which tend further to debilitate the already weakened patient. In addition to surface lesions, nodular masses commonly develop in the subcutaneous regions, particularly about the joints. In time many of these break down to form deep foul ulcers which are likely to give rise to hemorrhages of greater or less extent. Some superficial, warty growths may shrivel up and disappear and many larger ones undergo absorption, but the course of the disease may be prolonged over a period of many months by the development of new groups or crops of lesions, each outbreak usually being preceded by a recrudescence of fever and anemia.

**Etiology.**—Barton's bacillus is found in the local lesions, as well as in the red blood cells during the febrile period of the disease. These small, pleomorphic, motile, aerobic Gram-negative organisms, 0.2 to 0.5 μ by 0.3 to 3 μ, dumbbell shaped and coccoid, occur singly and in masses.

**Diagnosis.**—The symptoms are suggestive and the eruption is pathognomonic. The agglutinin titer is maximum just prior to the appearance of the eruption, when positive blood cultures may be obtained (Howe: AIntM 72 147 429 1943)

**Prognosis.**—The mortality averages about 15 per cent. Sluggish cases may drag along for months, and the patient finally recovers, while in those with hyperpyrexia, severe anemia, and great prostration, death may occur within a few days. One attack yields lasting immunity

**Treatment.**—Change of climate, particularly removal to the seashore, often proves beneficial. Treatment is largely symptomatic. Prevention is readily accomplished. It consists in staying away from infected regions, and in avoiding them particularly at night. DDT afford promise in control efforts.

## RHINOSCLEROMA

**Symptoms.**—Rhinoscleroma is a chronic granulomatous disease which affects the nose and upper repiratory tract. Women are attacked more commonly than men. Persons who live in poorer hygienic conditions appear to be more susceptible. The disease begins insidiously nasal symptoms being at first crusting and foul discharge, then obstruction and epistaxis. Diffusely or discretely there develop hard, insensitive, cartilaginoid plaques which are subcutaneous and later extend superficially (Cunning and Guerry: AOtol 36 662, 1942) The overlying skin gradually assumes a peculiar reddish or brownish, glistening hue and may become scaly and crusted. Within several months or years, the tumors tend to grow irregular or lobulated, with smooth or slightly wrinkled telangiectatic surfaces, and they are firmly embedded in the skin.



Fig. 210.

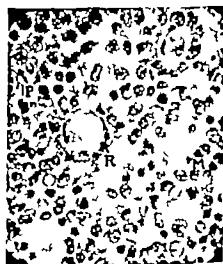



Fig. 211

Fig. 210 —Rhinoscleroma. (Dr R bert Andrade.)
Fig. 211.—Rhinoscleroma M Mikulicz cells R Russell body, which is a plasma cell showing hyaline, eosinophilic degeneration P plasma cells. (Dr Stuart Way)

Ultimately the masses diminish in size and become dense and hard. The resulting deformity depends on the location and extent of involvement. The disorder generally affects the anterior nares, uppe lip and contiguous structures, but cases have been reported in which the pharynx, larynx, trachea, tongue and even the lacrimal passages and the lobe of the ear were invol ed, either primarily or secondarily. In the nasal cases the nostrils are thickened and stiffened, and the tip of the nose is enlarged and elevated. Infiltration may be so great as t close the nares entirely. Mobility of the lips may be impaired so as to interfere with speech. The mucosa of the nose and pharynx becomes puckered and shrunken. The gums are involved in rare instances, and the teeth become loose and may fall out. Ulceration is rare, but may occur as a result of accidental injury or infection. The course of the disease is extremely tedious, extending perhaps over a period of many years. There is no lymph node involvement.

**Etiology and Pathology.**—It is possible that rhinoscleroma is due to a short, encapsulated, gram-negative bacillus isolated by von Frisch (1882) which is morphologically almost identical with the pneumococcus of Friedlander although the results of animal inoculation experiments have been negative. There is little evidence to show that the organism of v Frisch is primarily responsible for rhinoscleroma. There is no means by which it can be distinguished with certainty from other members of the encapsulated group, which are found in healthy noses (Topley and Wilson: Principles of Bacteriology 1937)

The tumor mass consists mainly of plasma cells, collections of which are irregularly scattered in all layers of the skin and subcutaneous tissue. The collagenous tissue is thickened and increased at many points in the tumor and it is this unyielding, fibrous material which accounts for the pathognomonic hardness of rhinoscleroma. Large, oval, dropsical cells, first described by Mikulicz, and hyaline degenerated cells of Pellizzari (Russell bodies) are characteristic regressive changes. Mikulicz's cells are probably degenerated plasma cells, each containing 6 to 8 of v Frisch organisms. The hyaline degenerated cells are spherical in shape, and like the dropsical cells are 4 or 5 times as great in diameter as the surrounding plasma cells.

**Diagnosis.**—The characteristic location of the lesions, their hardness, and the absence of ulceration, are suggestive. Syphilis carcinoma, other granulomas, and keloid are to be excluded by biopsy

**Prognosis and Treatment.**—The disease is steadily progressive and remarkably resistant to treatment. Surgical interference is usually followed by recurrence. Radiotherapy given early has proved palliative. A case was cured by streptomycin, 250 mg each 3 hours to a total of 97 gm., given because the Klebsiella group of organisms have been shown by Hellman (PSMMC 20 53, 1945) to be sensitive to this agent (Devine et al.: PSMMC 22: 597 1947)

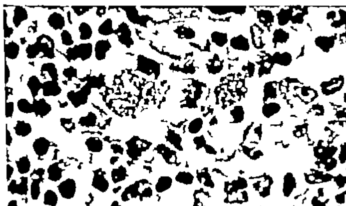


Fig 122.—Rhinoscleroma tissue showing Mikulicz cells (Simpson and Ellis AD&S 39 602, 1939.)

## ANTHRAX INFECTION OF THE SKIN

**Symptoms.**—Anthrax infection in the skin is manifested in a circumscribed carbuncle like, inflammatory lesion due to *Bacillus anthracis*. Anthrax in man may be septicemic or localized. The septicemic form generally is a result of spread from local infection of the skin. The infection may be immediate from the domestic animal or its hide or hair shaving brushes (J 117 115, 1941) or mediate through the bites of fleas, flies and other insects. The period of incubation ranges from 1 to 3 days. A small, pruritic, reddish macule resembling a flea bite develops t be followed in the course of from 12 to 24 hours by a red, indurated papule, which soon becomes vesicular or pustular The lesion often contains blood and soon ruptures, leaving a dark red base which dries and blackens within a few days. The sore is then a typical eschar surrounded by a vesicular zone The disease may proceed to recovery, or satellite vesicles may develop. The lesions are not necessarily of the textbook description.

**Etiology and Diagnosis.**—*B anthracis* may be found on apparently healthy animals. It causes disease in animals, however as well as in man. Anthrax is an occupa

tional disease among handlers of hides. Microscopic examination of smears suffices for diagnosis. *B anthracis* is ea y to cultivate (Lebowich et al. AmJClPath 13 803, 1943)

**Treatment.**—While early and radical excision of the lesions was at one time advocated, expectant treatment combined with specific serum gave better results (Hodgson: Lancet 1: 811 1941; Gold: Ann. IntM 0 783 194.) Immobilization, as in the treatment of carbuncle i an important measure Antianthrax serum can be obtained from the Bureau of Animal Husbandry at Wa hington, D C., and it should be administered repeatedly until edema begins t subside Sulfonamides have some value (Bonnar: BMJ 1 390 1940) but penicillin is now known to be paramount (Murphy et al : J 126 949, 1944 Ellingson et al. ib. 131 1105 1946) rendering other efforts, excepting isolation unnecessary

**Para-anthrax**, due to *B thracoid s* manifests accompanying lymphadenitis It does not respond to penicillin or sulfonamides (Epstein: ADS 57: 664 1948)

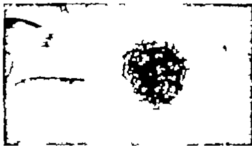


Fig 223.

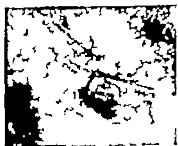


Fig 224.

Fig. 223 — Anth T kles cund black ulcer (Dr H Gold)

Fig 224.—Anthr pust l on neck, no longer edematous after treatment ith pecific tiserum, showing onl the olla of esicles bout the central ulcer (Gold JLCM 21 134 1935)

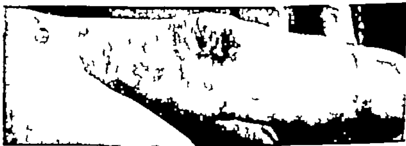


Fig 225.—Anthrax pustul on knuckl on fifth day of infection. (Dr Herman Gold)

## DIPHTHERIA OF THE SKIN

Cutaneous infection with *Corynebacterium diphtheriae* may result from autoinoculation contact with an infected individual or the use of contaminated articles. Cross infection of 16 of 18 patients on a ward was reported by Tauber and Goldman (ADS 4) 757 1942) Nasopharyngeal carriers are usually the source

The eruption often comprises gray sloughing ulcerating patches which develop around a swollen inflamed wound In many instances foci have been multiple and polymorphous eczematoid or pustular in character Genital lesions are not rare especially in girls Penile infection leads to sloughing sores of the glans (Crowther BMJ 2 646 1943) Umbilical infection in the newborn was reviewed with a collection of 66 cases by

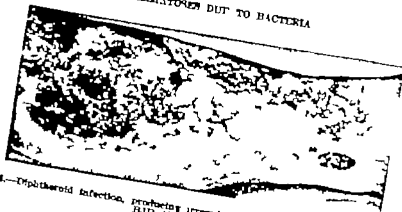


Fig. 226.—Diphtheroid infection, producing irregular ulceration of leg. (Barker et al BJD 49 360 1937.)

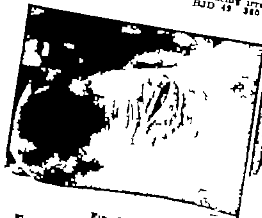


Fig. 227

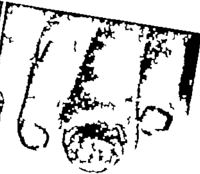


Fig. 228.

Fig. 227.—Pustular lesion of sole 5 ... duration. (Figs. 227-231 courtesy of Dr. R. Gill ADS 49 403 1944.)

Fig. 228.—Diphtheritic paronychia, 14 days' duration in a young girl. (Dr. R. Gill.)

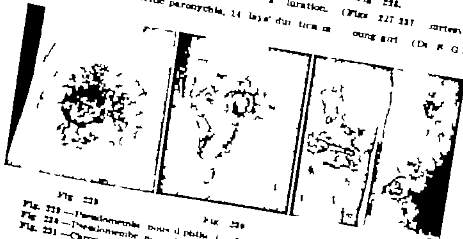


Fig. 229 Fig. 230 Fig. 231

Fig. 229.—Pseudomembranous diphtheritic ... of ankle ... after minor injury.

Fig. 230.—Pseudomembranous diphtheritic ulcer of ... days' duration. (Dr. ...

Fig. 231.—Chronic diphtheritic ulcer of 18 months' duration.

Thompson (BJChildDis 36 171 1939) Dermal lesions are usually ulcerative, but may resemble impetigo, intertrigo or varicella. When impetigo is associated with conjunctivitis, diphtheria must be suspected, for toxemia is not marked as a rule (Rogers IrishJMSc 150 283 1938) Impetiginous, purpuric, pyodermic and ulcerative lesions, in several instances accompanying diphtheritic conjunctivitis, were studied by Williams (BMJ 2 416 1943) who demonstrated virulence of the organisms in 12 of the 16 cases so tested.

See Livingood et al. (JInvD 341 1946) reviewing 140 U S. Army cases; Liebow et al. (AIntM 78 255 1946) neurologic complications and laboratory diagnosis; Denhoff and Koloday (ADS 55: 360 1947) relation to tropical ulcers. Church and Mason (ADS 56: 357 1947) diverse lesions of extremities, abdomen, genitalia.

Ulcerative lesions occurring in Palestine were intensively studied by Gill (ADS 49: 408, 1944; 51 243 1945) Occurring usually on the legs, the sores may be solitary

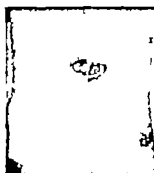


Fig. 232



Fig. 233.



Fig. 234.

Fig. 232.—Diphtheritic ulcer 16 days' duration, with rolled edges. (Dr S. Gill)

Fig. 233.—Desert sore with secondary diphtheritic infection, 6 weeks' duration. (Dr S. Gill)

Fig. 234.—Proliferating type of diphtheritic ulcer 7 days' duration. (Dr S. Gill)

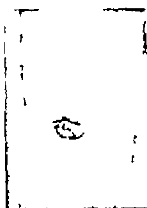


Fig. 235.



Fig. 236.



Fig. 237

Fig. 235.—Diphtheritic ulcer of 10 days' duration. Compare Fig. 236.

Fig. 236.—Same ulcer as Fig. 235, seen 8 days later (Dr S. Gill)

Fig. 237.—Scar of a diphtheritic ulcer which has been healed for a year (Dr S. Gill)

or multiple. They follow insect bites or minor trauma. A serosanguineous pustule may develop with a wide areola, pain, and regional lymphadenopathy. Or a pseudomembrane appears, beneath which necrosis and sloughing produce a punched-out ulcer. This loses its painful character in some 6 weeks, and cases are seen in which diphtheria is justly suspected as the original cause but only cocci can be found. Or proliferation of tender tissue follows rupture of the pustule, and a deep central cavity without membrane formation ensues. Erythema and pigmentation along with anesthesia about the ulcer are typical.

Multiple indolent ulcers, "jungle sores," in Indian troops were followed by weakness of the extremities, loss of reflexes, blurring of vision, and paresthesias (Ward and Mason BMJ 2: 253, 1945). To demonstrate the organism in ulcers, Cameron and Muir (Lancet 2: 720, 1942) removed the membrane, applied saline compresses for 24 hours, then scraped the surface at the margin to obtain material for cultures. They described acute early skin infections as small follicular blisters or pustules becoming flat sores while as a secondary invader *C. diphtheriae* caused the rapid development of a blackish membrane. Of their 66 cases with cutaneous lesions, 42 were limited to the skin and 13 developed paralyses. Deep punched-out ulcers seen in the South Pacific region were diphtheritic in many instances, reported Liebow et al. (ArIntM 78: 255, 1946). Trauma or an insect bite predisposed to the infection and the granulations at the bottoms of the ulcers constantly underwent necrosis. Slightly alkaline blood agar was good in bacteriologic identification, and penicillin in saline locally helped healing. The Schick test was twice as frequently positive in patients with such ulcers as in controls.

The Guillain Barré syndrome of upper respiratory infection followed by diplopia, paresthesias, disability of the lower extremities, high protein content but no other abnormality of the spinal fluid, and myocardial damage, is actually diphtheritic, and skin lesions may produce it, according to Delp (AnnIntM 24: 618, 1946). Myocardial involvement was better detected by electrocardiogram than by clinical examination, the more striking abnormalities occurring in the T waves; palpitation was not a symptom, but dyspnea and dizziness when erect, and abdominal pain, nausea, and breathlessness were noted by Kay and Livingood (BullUSAMD 4: 462, 1945).

**The Schick Test** is a means of distinguishing between the susceptible and resistant members of the human herd. It is performed by the intracutaneous injection of toxin, to which a positive reaction, an erythematous wheal, means antitoxin is absent or inadequate. The Schick test may not be relied upon as a definitive measure of immunity and repeated doses of toxoid should be given in prophylaxis (Bundesen et al. J 113: 1919, 1939).

**Diagnosis** depends on suspicion, suggestive clinical features, and in the end cultural identification of the organism and animal tests of its virulence. A test of dubious value consists in applying 2 per cent potassium tellurite to the lesion; blackening which develops in 5 to 10 minutes indicates the presence of diphtheria or diphtheroids (Marzullo BMJ 1: 1291, 1939).

**Treatment** requires isolation, penicillin locally and by injection, and antitoxin, 90 000 units intramuscularly with careful precautions against anaphylaxis (BullUSAMD March 1945). Antitoxin does not hasten healing. While *C. diphtheriae* is penicillin sensitive and the antibiotic should be given, antitoxin is equally necessary (Dodds BMJ 2: 8, 1946).

Danger is great to both the patient and his associates because of the likelihood of delay in diagnosis. Antitoxin given early and in adequate amounts is curative. Powdered methylene blue is a suitable topical application.

## PYOCYANEUS DERMATITIS

**Symptoms.**—*Pseudomonas pyocyanea* has occasionally caused an ecthymatous or gangrenous dermatosis. A patient with septicemic symptoms and abscesses which became gangrenous lesions simulating glanders was described by Carter (Lancet 1: 437, 1924). Infants and children, rarely adults, are affected, and undernutrition or cachectic states are predisposing factors. The lesions are livid indolent abscesses measuring up to an inch in diameter. They are multiple, develop rapidly and are capped by a vesicle or bleb, which ruptures to form a superficial ulcer with a necrotic center. *Ps. pyocyanea* may cause middle ear suppuration, ecthyma gangrenosum, necrotic and ul-

cerative lesions of the alimentary mucosa perhaps i fantile diarrhea. It is usually however merely nprophytic and occurs in feces and on the skin about the axillae and anus, commonly contaminating eczematous dermatoses and ulcers. It is sensitive to a id medium N reason is known to explain its occasional pathogenicity but our causal infections with this rganism are often associated with focal infection such as cystocele with chronic cystitis.

**Treatment**—Supporti e measures are recommended keeping the skin dry with alcohol and powders and the ulcers dry also with boric acid o other mild antiseptic preferably in powder form, while ultraviolet light and f reign protein therapy may be helpful. Weak solutions of acetic or citric acid or 0.5 per cent phosphoric acid are beneficial for local pplicatio (Weidman Appleton s System of Medicine 1937 Nap al YBD 1939 p. *00) Streptomycin sensitivity of *Ps. aeruginosa* was demonstrated by Bellow and Farmer (J 135 491 194 ) In experimental eye infections where m tillation of a solution of 10 000 micrograms pe c.c. were safe and effective. In dermatit of th ears, compresses a d instillatio s of ..500 unit per c.c. cured a case of Callow y (ADS 53 ..3 194 )

## NECROBACILLOSIS

An acute infect ous disease has been described in the human being caused by *B ecrophorus* a non spore bearing elongated gram variable filamentous anaerobe to which are attributed calf l phtheria, necrotic stomatitis of cattle foot-rot of sheep, gangrenous dermatit f h ses and mules, and hepatic necrosis of cattle pigs, and sheep (Beveridge JPathBact 38 467 1934) Bullae and erysipelas-like disease developed following a scratch f a meat inspector s hand, but recovery ensued after a stormy week, in the case f Stemen and Shaw (JKansMS 10 405 1910) No lymphangit or const tut onal ymptoms occurred the case of Darlier (BJD 53 231 1941) Subcutaneous abscesses of 8 years duration with gas formation characterized the case of Reuter (Trans ADA 1938)



Fig 228 —Necrobacillosis of the hand. (Dr F W Shaw )

## TUBERCULOSIS OF THE SKIN

Cutaneous infection with *Mycobacterium tuberculosis* may be primary or secondary the skin being involved by inoculation directly or from an internal focus Manifestations of tuberculosis in the skin depend on the presence and activity of *Myco tuberculosis* on its products, and on the reactivity of the tissues of the host This reactivity is a significant variable involving the newness of the infection or its superimposition on a background of previous infection which has altered immunity and sensitivity Immunity and sensitization are perhaps independent phenomena although the independence may be only partial as is shown by the fact that hyposensitization by injections of tuberculin does not necessarily alter immunity Clinical appearances vary according to the predominance and histologic location of the tubercules, the inflammatory process, the granulation tissue or the secondary changes such as hypertrophy or hyperplasia of the epidermis or degeneration, necrosis, or ulceration of the affected parts (Sulzberger and Wise MCNAm 14 1555, 1931)

Tuberculous lesions of the skin may be classified as follows:

Localized types of cutaneous tuberculosis, extending from an infected spot progressive in the absence of adequate immunity

1. Primary tuberculous complex in the skin (Ghon tubercle; inoculation into virgin soil)
2. Tuberculosis verrucosa cutis (inoculation into partly immune soil)
3. Tuberculosis cutis orificialis (secondary by implantation from disease of internal organs)
4. Scrofuloderma (secondary to subjacent glandular or osseous involvement)
5. Lupus vulgaris.

Hematogenous types of cutaneous tuberculosis.

1. Acute miliary tuberculosis (not limited to the skin, occurs usually in children, is generalized and fatal; immunity lacking)
2. Multiple disseminated tuberculosis of the skin (immunity inadequate to prevent caseation)
   a. Disseminated miliary lupus of the face.
   b. Rosacea like tuberculosis.
   Tuberculosis cutis indurativa erythema induratum tuberculous gumma.
3. Tuberculid with hyperergic immunity
   a. Lichen scrofulosorum.
   b. Papulonecrotic tuberculid.
4. Tuberculid with hypoergic immunit sarcoid; Schaumann's disease.

## Localized Tuberculosis Extending From an Infected Spot

**The Primary Tuberculous Complex** is characterized by the development of an ulcer at the site of inoculation accompanied by lymphangitis and lymphadenitis. Bacilli are present in the tuberculous chancre as well as in its satellite gland, which may or may not undergo caseation and ulceration. This syndrome occurs when tuberculosis is inoculated into virgin soil. (O'Leary and Harrison ADS 44 371, 1941 Epstein ib 51: 317 1945)

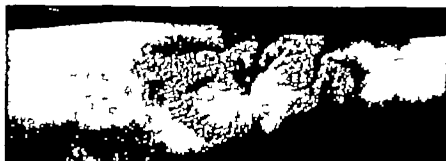
**Tuberculosis Verrucosa Cutis.**—Infection occurs from without as a result of inoculation, autogenous or from tuberculous cadavers, infected animals, and tuberculous sputum Sites of predilection are the exposed parts of the body The lesions begin with small, wartlike papules which gradually increase in number and coalesce to form small verrucose rounded, reddish brown patches. The lesions may heal spontaneously first centrally leaving thin, atrophic, whitish cicatrices.

VERRUCA NECROGENICA, or prosector's wart, is a form of tuberculosis due t inoculation. Lesions are seen most frequently on the dorsal surface of the thumb and fingers. They are usually indurated d alw v ke atotic The growths are persistent but benign, and disappear spontaneously w th but slight scarring if immunity is high.

**Tuberculosis Cutis Orificialis** attacks the integument contiguous with mucosal orifices. It begins with the formation of yellowish, miliary tubercles, which usually ulcerate to form sluggish, granulating painful sores. The progress of the disorder is slow The lesion is usually superficial with soft, irregularly outlined edges, and a raw uneven floor covered with purulent fluid. When the tongue is attacked, the patient suffers great pain and discommodation (Schugt Laryng 51 984 1941. Bryant AmRevTuberc 39 738 1939)

**Lupus Vulgaris** is characterized by plaques of small, soft, apple butter like tubercles. The malady progresses by the formation of satellite nodules, which coalesce to form irregular groups of various sizes. The face is the common site although no part of the body is exempt. The course is

Fig. 239



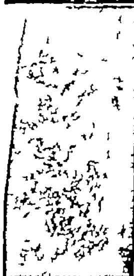


Fig. 240



Fig. 241



Fig. 242

Figs. 239-242.—Tuberculosis verrucosa cutis. Fig. 239 Antecubital (Dr Grover Wende) Fig 240. Forearm (Dr Robert Andrade) Fig. 241 Hand (Dr Henry Hazen) Fig 242. Hand (Dr D. E. H Cleveland)



Fig. 243



Fig. 244

Fig. 243.—Tuberculosis verrucosa cutis. (Dr J B. Shelmire.)
Fig. 244.—Tuberculous ulcer of tongue. (Dr George M. MacKee.)

slow but progressive. Regressions with subsequent atrophy may take place, but as a rule the lesions become small, crusted ulcers, which are ultimately replaced by fibrous tissue. Deformity resulting from ulceration, cicatrization and contraction may be great. The disease develops slowly and insidiously and the chronic course is characterized by periods of retrogression and exacerbation for many years. See Michelson (JInvD 7: 261, 1946) for historical review.



Fig. 245.



Fig. 246.

Fig. 245.—Lupus vulgaris. (Dr Grover Wende.)
Fig. 246.—Lupus vulgaris. (Dr D. E. H. Cleveland.)



Fig. 247.

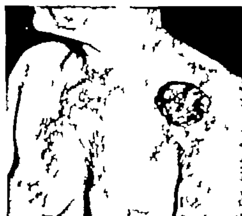


Fig. 248.

Fig. 247.—Lupus vulgaris. (Dr D. E. H. Cleveland.)
Fig. 248.—Lupus vulgaris. Squamous carcinomas following x-ray therapy.

**Scrofuloderma** comprises cases in which the skin is involved secondarily by direct extension from subcutaneous lymph nodes or bones which are tuberculous. Cervical lymph nodes are those most commonly affected. Infected nodes become swollen firm and adherent to the overlying skin They are at first nodular and elastic but later as a result of caseation may become doughy and ultimately fluctuant. Overlying skin becomes thinned, purplish and depressed and sloughs at *one or more points*. The resultant ulcers serve as mouths of sinuses from which purulent matter discharges. The sinus walls are soft reddish and granular and bleed readily Symptoms are trivial, and constitutional manifestations are slight The lesions may heal spontaneously with the formation of rough, corded cicatrices, or the disease may persist for years with little change. Most patients are children and young adults.



Fig. 249



Fig. 250.

Fig. 249 —Scrofuloderma. (Dr Robert Andrade.)
Fig. 250 —Tuberculous gummas (Dr D F H. Cleveland.)

**Pathology** —*Mycobacterium tuberculosis* gives rise to histologic changes in the dermis which do not differ from those resulting from its presence in other tissues of the body The essential lesion is the tubercle or tuberculous nodule The epidermis is not involved primarily but is usually stretched and thinned as a result of pressure from below Bacilli are numerous in lesions associated with low immunity and scarce in those with hyperergy They may be undemonstrable in hypoergic individuals whose immunity is high.

Researches using chemical fractions of dead tubercle bacteria (Sabin and Joyner J Exper M 68 639 83 1938) prove that specific fractions evoke typical responses. The phosphatid substance injected subcutaneously provokes an epithelioid and giant cell reaction the waxes, proliferation of fibroblasts the acetone soluble lipid, proliferation of all connective tissue cells including those of the vessels, even causing hemorrhage the polysaccharides are chemotactic and toxic to leucocytes; the protein

produces plasma cell proliferation and fever Tissue responses depend also on factors of sensitization and immunity that are incompletely understood (see Rich Pathogenesis of Tuberculosis, Thomas 1944 Friedman: AmJPath 22 621 1944 asteroid bodies in giant cells of sarcoid) Explants from an immune donor retain acquired immunity which appears to be concerned with fixed tissue cells, mononuclears and phagocytes, but no circulating antibody is demonstrable (Edit. J 119 1508 194_)



Fig. 231.



Fig 232.

Fig. 231.—Tuberculous tissue from a miliary sarcoidal lesion, howing giant cells and epithelioid cells, but no caseation.

Fig. 232.—Lichen scrofulosorum, showing tuberculous inflammation superficially located in the dermis. (Dr Stuart Way)

**Diagnosis of Tuberculosis Cutis.**—So various are the clinical con figurations under which tuberculosis may appear that as in syphilis, suspicion of its possible existence and broad knowledge of its manifesta tions are required for diagnosis. (Montgomery ADS 35 698, 1937 types and classification.) Biopsy and animal inoculations are two reliable means for diminishing equivocation. Tuberculous lesions are to be differentiated from those of carcinoma, syphilis, lupus erythematosus and blastomycosis. In lupus vulgaris the nodules develop in previously sound skin and are always soft and compressible. Under a pressure glass outlying tubercles appear as yellowish, apple-butter-colored puncta surrounded by exsanguinated sound skin. Tuberculous ulcers have soft nonelevated margins, and their bases are usually granulating and pliable Most apparently normal adults show strong reactions to tuberculin having met the infection and subdued it. A negative test may signify positive or negative anergy Quantitative intradermal testing has significance (Bon nevie et al. abs YBD 1940 p 551) Tuberculin patch tests are simple, harmless, and fairly reliable (Vollmer and Goldberger AmJDisChild 57 1272, 1939)

**Prognosis of Tuberculosis Cutis.**—Lupus vulgaris is extremely chronic rebellious to treatment and prone to relapse and recur The development of cancer in old lupus cicatrices is common age and x ray treatment favor its development Systemic tuberculosis is present or develops in a considerable proportion of the cases. The outlook in miliary

and disseminated tuberculosis is even graver Tuberculids are benign in themselves, but they may signify an awakening of the systemic disease.

**Treatment of Tuberculosis Cutis.**—Hygienic measures are important in this form of the disease, as in systemic infections. Fresh air sunlight, ample nourishing food and moderate exercise are helpful. Some authorities have made use of a salt free diet. It is alleged at times to produce results that surpass those of any other method of therapy (Blumenthal and Funk Strahlenther 45 49 1932) Tuberculin, capable of doing much harm, was once discarded as being of no use. MacKee (JCutDis 29 397 1911) found it valuable in nonulcerating lupus and tuberculosis verrucosa cutis, and least effective in the ulcerating forms. The dose is increased progressively but not to the extent of producing fever Gold sodium thiosulfate or other salts may be given intravenously Gold is beneficial in some cases, but intoxication must be carefully avoided.

Streptomycin will usually induce fairly prompt, apparent cures of skin lesions, but histologic tuberculous changes persist, and disconcerting disseminations of tuberculous disease such as meningitis and peritonitis have *followed* its administration If streptomycin is given the minimum dose should be 2 gm. per day said O'Leary et al. (ADS 55 222, 1947) and most benefit accrues in scrofuloderma See Council Rpts (J 135 634 1947 138 584, 1948 Veterans Administration hospitals experience) 1 gm per day suffices. Toxic manifestations, especially labyrinthitis, necessitated stopping the antibiotic in 6 per cent of the series.

Vitamin D is reported (Dowling and Thomas BJD 58 45 1946) to yield remarkable improvement in lupus vulgaris and is usually tolerated in a dose of from 200 000 to 400 000 units per day but entails hazard of metastatic calcification of kidneys and vessel walls as well as less consequential symptoms of intoxication Macrea (BJD 59 33 1947) obtained excellent improvement in most of the 20 cases of lupus vulgaris so treated. Michelson and Steves (ADS 56 317 1947) helped 6 cases, obtaining scarring fibrotic healing with a dose of 150 000 units of viosterol in oil per day Toxic reactions (Bills PhysRev 15 1 1935) include nausea anorexia, vomiting cramps, diarrhea urinary frequency tenderness of gums and teeth, arthralgia and myalgia, dizziness, weakness, headache, haziness of memory and paresthesias of the extremities. Inactivated ergosterol is nontoxic and is as beneficial in a dose of 300 to 500 mg. per day intramuscularly as vitamin D wrote Raab (Sc 106 546, 1947) A rise in serum calcium follows $D_2$ treatment and is a good indication of incipient toxicity (Dawson BJD 60 164 1948) Yet the remarkable effects of improvement are most marked during the toxic phase of the administration of the drug (Edit. BMJ 1 455 1948) During healing the tuberculous tissue diminishes and is replaced by young connective tissue (Freudenthal BJD 60 178 1948)

Roentgen therapy heliotherapy and phototherapy are efficient methods for local attack Phototherapy by means of the Finsen lamp gives the best cosmetic results but is extremely tedious It requires great patience and a staff of trained specialists (Lomholt BMJ 2 291 1934 Edit. *BMJ 2 366 1943*) *Aitken (BMJ 1 160 1937) used* carbon arc light baths with especially good effect in the glandular cases.

Destructive agents of many kinds have a place in the treatment of lupus vulgaris Acid nitrate of mercury applied to the nodule by means of a small swab produces necrosis, crusting superficial chemical ulceration and sloughing of the tubercle which eventually heals with scar Trichlor

acetic acid, lactic acid, potassium permanganate crystals and electrocoagulation are among the agents that have been used (Cipollaro APhysTh 18 415 1937)

### Hematogenous Types of Tuberculosis of the Skin

**Acute Miliary Tuberculosis.**—Eruptions may or may not be present Purpura may occur The infection is overwhelming and the tuberculin reactivity is likely to be anergic (Rubin AmRevTuberc 39 567 1937)

**Multiple Disseminated Tuberculosis of the Skin.**—The lesions are small, circumscribed collections of brownish scale-covered nodules which appear suddenly and are irregularly distributed over the face, trunk, and extremities. They may undergo central caseation necrosis so as to form ulcers, which heal slowly

**Miliary Lupus of the Face** is a disseminated form in which tubercles, scattered more or less symmetrically on the face, are manifest as small, yellowish, discrete papules. They make their appearance sometimes coincidentally with an exacerbation of pulmonic tuberculosis. The eruption is chronic, unsightly but asymptomatic. It favors the periorbital regions. Histologically the lesions show caseous tuberculosis. The patients react to tuberculin with moderate hyperergy Animals have been unsuccessfully inoculated with material from the lesions. (Wise and Satenstein ADS 4 544, 1921.)

**Rosacea-like Tuberculosis** is characterized by minute, discrete, brownish or dusky red, flattened, papular lesions on the face. They make their appearance suddenly and in crops, and persist over a considerable period of time They differ from the lesions of rosacea in being not centrally located upon the face, not usually pustular and not accompanied by seborrhea. Intravenously administered gold sodium thiosulfate may yield prompt therapeutic effects in this disease. Sensitivity to tuberculin is usually high, though Laymon (ADS 54 231, 1946) found such variation of reactivity in Minnesota cases that he judged the test of little diagnostic importance. See Laymon and Michelson (ADS 42 625 1940)

**Tuberculosis Cutis Indurativa** includes erythema induratum and similar clinical groups of tuberculous disease in which scattered nodular lesions occur the microscope revealing caseating tuberculous structure.

**Erythema Induratum (Bazin's Disease)** is characterized by the development of symmetrical indurated cutaneous nodules which terminate in absorption or necrosis. The patients are often girls or women with "chilblain" circulation. The lesions develop insidiously They are usually confined to the legs, particularly the calves and the lower third of the thighs. The nodules develop in the panniculus adiposus and first become apparent to the touch as rounded or oval pea to cherry size, indurated masses which are slightly tender on pressure, and tightly adherent to the overlying skin, which assumes a reddish or purplish hue. Many undergo spontaneous involution, leaving discolored, reddish or brownish spots which persist. The mass may ulcerate, but necrosis is circumscribed as a rule and the process is comparatively superficial. Tuberculous erythema nodosum probably represents more successful inflammatory reaction to bacteria than erythema induratum.

TREATMENT.—Disseminated tuberculosis is a persistent malady undergoing relapses and recurrences. Rest with elevation of the affected parts, is a valuable measure Cod-liver oil generally is indicated. Curettage may be advisable in ulcerative cases. Baths in ultraviolet or carbon arc light are beneficial.

**Nodular Lesions of the Legs.**—O'Leary (ADS 50: 212, 1944) described nodular vasculitis productive of scarring lesions in two middle-aged women. Montgomery et al. (J 128 335, 1945) reviewed 175 cases of nodular sometimes ulcerative, lesions

of the legs and 40 cases of recurrent idiopathic thrombophlebitis. While histologic structure suggesting tuberculoid may prove a false suggestion, yet tuberculous disease proved by animal inoculation may manifest only nonspecific inflammatory reaction, they believed. Diagnosis of tuberculous nodules was accepted if guinea pig inoculation was positive, histologic structure was tubercle, tuberculosis elsewhere in the body was demonstrable by roentgenologic finding or strongly positive tuberculin reaction, and the ulcerative appearance and course after prolonged observation were typical. Among their distinctions which were argued as not valid by Anderson (J 123: 1248, 1943) they thought nodular vasculitis more painful than erythema induratum, which occurs in younger women. The debatable status of nodular vasculitis serves to emphasize the fact that some lumps in legs are not tuberculous and that diagnosis should be critical even if difficult. See erythema nodosum p. 501

**Tuberculids.**—The term tuberculid indicates, and should be restricted to, an eruption due to a shower of tubercle bacilli reaching the skin by embolism in persons with high tuberculous allergy said Rothman (ADS 54 231 1946) Lichen scrofulosus, papulonecrotic tuberculid, and erythema induratum conform to this definition We see no sound semantic reason for excluding other eruptions, including those which are sarcoidal presumably because of positive anergy if they are due to showers of tubercle bacilli also The following descriptions fit certain varieties of tuberculous manifestations.



Fig 233.



Fig. 234.

Fig 233 —Miliary tuberculosis of the face. (Dr L. W Ketron.)
Fig 234 —Miliary sarcoidal tuberculosis of the Negro.

**Hyperergic Tuberculids**—Such doses as 0 1 c c. of 1 1 000 000 dilution of tuberculin result in reactions when injected *intracutaneously* in certain persons. The conception of hyperergic tuberculids is based on the existence of such sensitivity (Low EdinMJ 39 154 1932)

These eruptions are thought to be due to multiple emboli of bacilli of low virulence which rapidly ... in the tissues. Clinical manifestations depend on the quantity of the toxic material and the sensitiveness of the skin. Eruptions are better called true tuberculosis if organisms are demonstrable in the lesions microscopically or by animal inoculation. Tuberculid implies absence of demonstrable organisms; occurrence in phthisical subjects a histologic resemblance to that recognized for tuberculosis; and perhaps, as in lichen scrofulosorum, experimental production of

the disease by injection of tuberculin. Tuberculous di ease in the skin may be divided into (1) true tuberculosis, ( ) tuberculids, and (3) sarcoid forms. In true tuberculosis, there is classic tubercle formation caseation occurs, organisms are present and reactivity is hyperergic In tuberculids, there is typical tubercle formation histologically and reactivity is hyperergic, but organisms are not present. In sarcoid forms, the tubercle is naked (epithelioid structure) organisms are lacking, and the reactivity is hypoergic, even anergic.



Fig. 213.—Tuberculosis cutis indurati a. (Drs. Fordyce and MacKee.)



Fig. 214.—Erythema induratum. (Drs. Fordyce and MacKee.)

**Lichen Scrofulosorum** is characterized by the occurrence of asymptomatic groups of pinhead size pinkish or reddish, desquamat ng papules. The lesions are little conical papules, which tend t form rounded, superficial plaques which ult mately disappear without scar The sit of pred lection is the trunk The lesions ha ppeared following injections of tuberculin. React ity t t berculin is high. Demonstrable bacteria are absent. The lesions generally disappear under ppropriate treatment Phlyctenular keratitis is an occasional complicat on.

The disorder responds t large doses of tamin A.

**Papulonecrotic Tuberculid** manifested w th small, discret lesions f widespread, generall symmetric distribution They appear in crops and are apparently

due to the dissemination of tuberculous antigen via the blood stream. Since animal inoculations are regularly negative, the antigenic substance may be either enfeebled circulating bacteria or bacteria killed in the tissues, where they are not to be found microscopically. The tuberculin test is positive in extreme dilution. The individual lesions are of various sizes, but are always small. They begin as tiny papules, which enlarge slightly, become somewhat tender, undergo central necrosis with sloughing or



Fig. 237.—Papulonecrotic tuberculid, active lesions and atrophic scars. (Drs. Fordyce and MacKee.)



Fig. 238.—Papulonecrotic tuberculid, atrophic scarring. (Drs. Fordyce and MacKee.)



Fig. 239.—Lichen scrofulosorum. (Dr. T. C. Gilchrist.)

crusting, and eventually heal with the production of circular, sharply demarcated scars, which are white, atrophic, and slightly depressed. Extensor surfaces of the extremities are the sites of predilection. Itching is absent, a distinction from prurigo. Manifestations in the Negro were described by Irgang (ADS 47: 627, 1943; 53: 372, 1946). See Pautrier and Worringer (BSocfrancD 46: 413, 1939).

**Hypoergic Tuberculids (Sarcoid)**—The lesions are typically composed of epithelioid cells, but giant cells, bacteria and caseation are wanting. Immunity is high, but allergic reactivity is slight. Since specific organisms are not ordinarily demonstrable, doubt exists as to the specificity of the cause and there is justification for believing that several etiologic agents are capable of provoking sarcoidal tissue reaction. Both tuberculosis and leprosy probably produce sarcoid, and there is no reason for insisting that these two infections conclude the list (Jordan and Osborne ADS 35 663, 1937 Irgang ib 40 35 1939)

**Sarcoid in the Skin** is characterized by the presence of few or several sharply defined, elastic, brownish intracutaneous and subcutaneous nodules which are asymmetrically distributed over the face or extremities or both. The tumors are benign. When they undergo involution, either spontaneously or as a result of roentgen therapy they may leave no trace or a pigmented spot, or a thinned, atrophic, macular cicatrix. Clinical varieties are large nodular small nodular or papular and diffusely infiltrating. Cases may be atypical or mixed. The skin tumors may range in number from 1 or 2 to 100 or more. The face is the site of predilection. The lesions usually begin as minute firm, rounded nodules which may appear in crops but develop slowly. The surface is covered by a fine network of capillaries. After attaining a size from that of a split pea to that of a walnut, and persisting for months or years, the growths may undergo regression. They almost never ulcerate.

**Sarcoid a Systemic Disease.**—Schaumann (BJD 48 399 1936) collated evidence that sarcoid may be (and generally is) a disease of wide dissemination in the lymphohematopoietic system. He applied the name lymphogranulomatosis benigna to cases characterized by (1) lymphadenitis in the neck, axillae, or groin, (2) epithelioid tubercles in the tonsils, (3) fusiform swellings of the fingers and toes due to sarcoid within the bone marrow and demonstrable radiographically as cavernuform and osteoporotic lesions and (4) skin lesions at first of the type described above, later becoming more like those of lupus pernio, but with (5) a possibility that skin lesions might not be present at all.

Involvement of internal organs is part of the disease at times the entirety of it, while the complete syndrome with cutaneous, osseous, lymphatic, and visceral lesions is found in comparatively few patients the majority of whom manifest pulmonic and lymphatic lesions. Reisner's review of 35 cases with 4 necropsies is worth study (AmRevTuberc 49 289 1944) Mainly young adults, 30 were Negro and 5 white. The lungs were affected at least to some extent in 33 with mild nonproductive cough and minimal physical signs. Chest films revealed (1) diffuse, disseminated small nodules as in hematogenous tuberculosis, or (2) diffuse or local strandlike changes following the bronchovascular markings, or (3) patchy coalescent densities suggestive of conglomerate fibrotic induration, usually associated with types 1 and 2. Lymph nodes were usually discrete, movable nontender and moderate in size. Mediastinal and tracheobronchial enlargement was present in 30 cases, typically with widening of the superior mediastinal shadow and prominence of the root areas, usually bilateral and often symmetric, generally without symptoms or signs. Thoracic studies of value were recorded by Bernstein and Sussman (Radiol 44 37 1945)

Osseous changes, demonstrable in the smaller long bones, particularly the digits and ribs, are those of osteitis fibrosa cystica, and are found in perhaps a fourth of the cases (Connolly BJRadiol 11 23, 1938)

Myocardial lesions occurred in the patient of Cotter (AIntM 64 286 1939) Pituitary damage in the patient of Barber (BJD 53 70 1940) caused changes simulating Simmonds's disease and was alleviated by implant of desoxycorticosterone and testosterone. Some cases of uveoparotitis and Mikulicz syndrome are in reality sarcoidal (Pinner: AmRevTuberc 3 690 1938) Renal and retinal damage featured the unusual case of Klinefelter and Salley (BullJHH 79 333, 1946) See also Lambie (MJAustral 1: 815, 1940) review; and Pautrier (La Maladie de Besnier Boeck-Schaumann, Masson, 1940)

The disease starts early in adult life and progresses insidiously bearing a superficial resemblance to Hodgkin's disease. Guinea pig inoculations are almost invariably negative until late, when the patient may eventually succumb to active tuberculosis. Schaumann (1936) despite extensive inoculation experiments was unable to cultivate the tubercle bacillus from his patients although 4 of them came to autopsy. Schaumann and Hallberg (abs YBD 1941 p. 487) were able to find tubercle bacteria in the tissues



Fig. 260



Fig. 261

Fig. 260.—Disseminated tuberculosis of the f ce (Drs. Fordyce nd M cKee.)
Fig. 261.—Sarcoidal lesions in skin of f ce.







Figs. 262-264.—Sarcoid of Schaumann. I the neck are nodules, cystic abscesses and sinus tracts. In the skin re discrete, scaling coppery infiltrated lesions in groups. Histologically the lesions show noncaseating groups of epithelioid cells.

with Hallberg staining method. Cameron and Dawson (EdinMJ 53: 463, 1946) supported the theory of tuberculous etiology with their case. Of cases long watched by Reisner 12 regressed, 9 progressed, and 5 remained stationary. He believed the outlook dependent largely on the extent of permanent functional damage of the organs involved, while frank tuberculosis accounts for most of the fatalities.

Plasma globulin i increased in sarcoid (Salvesen 1935 confirmed by Longcope: J 117: 1321 1941). Hyperproteinemia due to increase of globulin returns toward normal as the patient improves, and is of prognostic significance (Fisher and Davis BullJHH 71: 364 194_)

Histologically the nodules consist f sharpl defined collections of epithelioid cells with pale-staining nuclei, the masses being separated by connective tissue septa, within the meshes of which there may occur few giant cells and lymphocytes. The nodules contain vessels, but no elastic tissue. The epithelioid infiltration is the same in the skin, tracheobronchial glands, lungs, bones and viscera. Epidermal changes if present are secondary.

In the treatment of sarcoid neoarsphenamine has been thought beneficial and cod liver oil should be given. X-ray therapy will bring about resolution of the skin lesions as a rule; small doses suffice. X ray did not help the lymph node involvement in cases of McCort et al. (AIntM 80 293, 1947). Chaulmoogra oil, 3 t 9 c.c intramuscularly each week, was recommended by Orm by (ADS 50 61 1944). Old tuberculin may help when started with 0.1 c.c. of 1 1,000,000, gradually increasing the dose at to 3 week intervals. Calciferol therapy given as for other forms of tuberculosis, induced marked improvement in 2 cases of Curtis et al. (JInvD 9 131 1947) in which increased excretion of phosphorus wa noted and toxic symptoms developed.

THE KVEIM TEST (REACTION).—Sarcoidal lymph node tissue crushed under aseptic conditions, mixed with saline, diluted 1:10 and filtered through gauze sterilized at 60° C. for hours and tested for sterility by aerobic and anaerobic culture and guinea pig inoculation, is phenolated (0.5 per cent) and serves a the antigen (Danbolt ActaMVenol 114 143, 1943). One injects 0.1 to 0._ c.c intracutaneously and observes the test site for several months. Positive reaction is indicated by the development, after about two weeks, of persisting erythema and induration, reaching its max imum in t o months then fading slowly (Leider JInvD 10 377 1948). The positive test site shows sarcoidal structure histologically. The test is usually positive in persons with active sarcoidal disease and negative in healed or inactive cases (Nelson JInvD 10 15, 1948). It has prognostic as well as diagnostic value.

**Unusual Tuberculodermas** occur and mixed cases are common. Both the usual forms and the unusual are fairly well comprehended if one keeps in mind the possibilities which may result from variations in virulence of organisms and in responsiveness of the tissues of the host. Sarcoidal structure results from comparatively good immunity (positive hypoergy) and necrosis results from high reactivity (allergy) or else from damage by virulent bacteria (negative hypoergy). The multiformity of syphilis is scarcely greater than that of tuberculosis (Montgomery MCNAm 19 611 1935 Blumenthal ADS 35 1037 1937)

## LEPROSY

Leprosy is a disease believed to be due to infection with *Mycobacterium lepræ* Hansen s bacillus. While Koch s postulates have never been fulfilled (Edit. InternatMDig 37 254 1940) this acid fast organism similar in many respects to *Myco tuberculosis* apparently provokes chronic inflammatory disease of tuberculoid histologic structure with acute exacerbations, or lepra reactions, by altering reactivity and by invading and destroying cutaneous and peripheral nervous structures. Noteworthy similarities exist between leprosy and tuberculosis.

**Symptoms** are variable for skin or nerves or both, in differing degrees, may be damaged. Three clinical forms are recognized (1) Lepromatous, the nodular form (2) Neural the macular or anesthetic form, and (3) Mixed *lepromatous and neural forms*.

Cases are classified as neural (N) and lepromatous (L). Degrees 1, 2, and 3 signify slight, moderate, and advanced. A mixed case with moderate cutaneous and slight neural symptoms would accordingly be designated L-2, N-1. The terms "active," "quiescent," and "arrested" are used, but not the term "cured." The distinction between neural and cutaneous lesions in the skin may be dim; the lesions may be called "cutaneous" if bacteria are sufficiently numerous to be found. The mixed type is more common than either of the others because most nodular cases show some evidence of nerve involvement within a few months, although many neural cases never show nodular lesions at any time.

The classification favored by South American authorities (Pardo-Castello and *Tiant: J 121: 1264 1943*) is based on pathologic changes: lepromatous structure with foam cells and numerous bacilli corresponding to lack of immunity, lepromatous lesions and bad prognosis on the one hand and tuberculoid structure with epithelioid cells and rare bacilli only in exceptional instances corresponding to good immunity, small nodular lesions and favorable prognosis on the other hand. There is, in addition, simple nonspecific inflammation representative of macular and dystrophic clinical lesions.

The nerve lesions are tuberculoid in structure and all lepers have at least some nerve involvement, according to Pardo-Castello et al. (AD 55: 783, 1947). In tuberculoid leprosy the nerve lesions are miliary tuberculoid or sarcoidal and there are many giant cells. These lesions terminate in fibrosis and destruction of nerves. "Neural" and "cutaneous" forms designate only location of lesions.

The incubation period may last 5 to 25 years, and the initial signs may long go unrecognized. After the body has been invaded, there occur febrile reactions due to heightened reactivity. Febrile reactions accompany the appearance of new lesions, the aggravation of old ones, or both. During an exacerbation there may appear eruptions resembling erythema multiforme. The final stage of the disease exists when elimination is finished and atrophy has replaced granulomas. Osseous changes radiologically demonstrable occur in perhaps 95 per cent of the cases.

In addition to the small foci in New Brunswick and Manitoba, Louisiana, Texas, and Florida contain the majority of the North American cases although sporadic importations are not very unusual in the Pacific and Atlantic seaboard cities. The disease is increasing in incidence in the United States. Data on 723 patients studied in the previous 15 years at the National Leprosarium at Carville, La., U. S. A., were collated by Hopkins and Faget (J 126: 937, 1944). Of these 303 were foreign born and 420 were natives of the U. S. A. Patients from Mexico, the Philippines, British West Indies, and China accounted for [illegible] per cent of the foreign-born, and many of these had probably contracted the disease abroad, possibly thereafter establishing foci responsible for some native-born cases, especially in Texas, California, and Florida. New York and Illinois cases probably were imported, and the decline in admissions from Minnesota and Massachusetts suggested that leprosy is not indigenous there. Veterans of foreign wars probably contracted their infections overseas. The average age on admission was 35.5 years. The average age at onset was 30.4 years. Whites were twice as numerous as Negroes from Louisiana. Males outnumbered females more than 2 to 1 on the average, but Negro males and females were approximately equal. Mixed leprosy cases almost equaled the total of the others, but lepromatous outnumbered the neural. A family history of leprosy was found in 147 patients, but there were only [illegible] marital couples, indicating that close contact is not the sole factor in transmission. Occupation did not appear to be an etiologic factor. The first lesion was described as a macule by [illegible]30 patients and a nodule by 193, but the sites of these did not hint at the portal of entry. Other initial manifestations comprised sensory disturbances, usually anesthesia, or blisters, painless burns, and plantar ulcers. Serologic tests were without value in distinguishing leprosy from syphilis. The average duration of life after the onset of leprosy was calculated as 10.3 years but [illegible]0 per cent of the patients had been released conditionally as arrested cases. No tuberculoid case had relapsed, but relapses had occurred in a tenth of the neural cases, an eighth of the lepromatous, and a fourth of the mixed. Leprosy was rarely responsible for fatalities but nephritis and tuberculosis were the direct cause of almost half the deaths.

**Lepromatous (Nodular) Leprosy.**—Skin lesions usually begin as ill-defined reddish macules. Later the skin becomes infiltrated, thick



Fig. 265.



Fig. 266.

Fig. 265.—Lepromas of ea nd face. (Drs. Morrow Miller and T weig.)
Fig. 266.—Advanced lepromatous leprosy (Dr F G. Reimertz)





Figs. 267 and 268.—Leprosy nodular and anesthetic. (Dr J A. J hnston.)

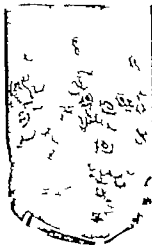


Fig 269.



Fig 270.



Fig 271

Fig. [illegible].—Psoriasiform leprid (Costa BJD [illegible] 242, 1948.)

Fig 270 —Leprosy, with keratitis, interosseous muscle trophy and trophic ulceration of digits. (Dr J A. Johnston)

Fig. 271.—Lepromatous lesions of face and trophy contractures nd digital ulceration of hands. (Dr O. G. Costa.)

ened and nodular The symptoms of constitutional involvement are *generally ill-defined and void of diagnostic significance*, but these and the changes in the upper respiratory mucosae are among the early manifestations. The macules are commonly devoid of hair The course of these lesions varies greatly Many disappear often leaving brownish pigmentation a few usually persist and may ultimately become infiltrated but nodules which subsequently appear commonly develop independently Nodules are rounded or oval in outline brownish in color and firm in consistency They may disappear spontaneously and be succeeded by another crop of tumors, or they may persist unchanged, or they may progress, enlarge and ulcerate. While the course of the disease is steadily progressive remissions are common, especially in the early stages. Healing *may supervene with the formation of flexible cicatrices or hypertrophic* fibrous masses. Or the ulcers may persist indefinitely their raw surfaces partially covered with thick brown crusts. The face and forehead are favorite sites of leprous nodules, and thickening and infiltration of the skin in this region often give rise to great deformity leontiasis.

The neural macule is anesthetic to light touch the cutaneous is not Sarcoidal leprous lesions in the skin have disturbed sensibility (Reenstierna abs YBD 1940 p 203)

**Neural (Anesthetic) Leprosy** is the less virulent type of the disease The bacteria evince preference for the neuroglia of the nerve trunks, and predominant symptoms result from neuritic changes. The course is *slow many years perhaps being required for development of characteristic* symptoms The great auricular ulnar and peroneal nerves become palpable and tender comparatively early In many cases it is easy to see such nerves beneath the skin when the parts are suitably stretched. As atrophy succeeds irritation of the nerve trunk, its ability to convey sensation is lost. The characteristic cutaneous eruption consists of oval or irregular brownish sharply-defined macules which range from 3 to 10 centimeters in diameter and are distributed over the limbs and trunk. At first they are slightly pruritic but they eventually become anesthetic. Bullae frequently develop but usually rupture quickly although there may be some resultant scarring Trophic changes occur both in the vicinity of the patches and in other tissues of the affected limbs. The skin becomes thick, dry harsh, and inelastic The hair on the affected areas loses its pigment Being anesthetic the patients frequently injure the parts unconsciously and ulceration and infection are usual simulating syringomyelia. Ultimately owing to paralysis and atrophy of the extensor muscles of the forearm and the interosseous muscles of the hand the fingers may become flexed and immovable (leper claw) Absorption of bone usually begins in distal phalanges and rarely involves a long bone Blindness is common, resulting from corneal anesthesia and ulceration or less often from ocular leproma (Prendergast AOphth 23 112, 1940)

**Mixed Type.**— A case is often distinctively tubercular or anesthetic but gradually develops symptoms of the other variety Occasionally the case is a mixed one almost from the beginning

**Etiology** — The mode of inoculation is not known There is some evidence that *M leprae* is a soil organism and that leprosy is a soil infection. Apparent inoculation by tattooing was reported by Porritt and Olsen (AmJPath 23 805 1947)

The organisms are perhaps to be found in nasal discharges. They are present in immense numbers in ulcerated lepromas. In some neural cases,

the only way to find the organism is to scrape the nerve or to excise a part of it. Infection occurs usually only after prolonged and close contact. The disease is not highly infectious. Familial transmission is fairly common.

**Pathology**—Leprous nodules consist of masses of connective tissue cells, with intermingled lymphocytes, plasma cells, and mast cells. Scattered through the lesion are variable numbers of large, ovoid cells, the lepra or foam cells which contain acid fast bacteria. Macules in the anesthetic type of the disease contain few demonstrable bacilli, but contiguous nerve trunks are always involved (Lehmann ADS 37 175 1938). All active leprids show tuberculoid histologic structure whether neural or otherwise (Wade et al InternatJ Lepr 5 1 285 437 1937 6 199 1938). A triple stain revealed granular zoogleal sporelike forms but not rods in neural and tuberculoid cases, reported Jackson (Sc 101 563 1945). Lymph nodes, especially of inguinal and axillary regions, show lepromatous structure and contain bacilli in 96 per cent of the lepromatous cases, and show tuberculoid structure with bacilli less frequently demonstrable in tuberculoid cases (Schujman and Vaccaro abs YBD 1943 p 333).

**Diagnosis**.—The rule adhered to by the United States Public Health Service is to find acid fast organisms in the skin lesions rather than on mucous surfaces. In nerve cases, in which acid fast organisms may not be found, there at least must be anesthesia and other evidence of peripheral nerve involvement before a diagnosis on clinical symptoms alone is permissible. According to most leprologists, cases in which acid-fast organisms cannot be demonstrated are of little, if any menace to other persons.

One must distinguish syphilis, mycosis fungoides, lupus vulgaris, syringomyelia, Raynaud's disease, morphea and vitiligo. Syphilitic lesions usually pursue a comparatively rapid course, and never exhibit sensory changes. The characteristic infiltrations of leprosy are wanting even though the history of exposure be present. Dependence cannot be placed on serologic tests for syphilis, for they are often positive in leprosy (Hazen et al. VDI 17 253 1936). The lesions of morphea, vitiligo, and Raynaud's disease are unattended by sensory changes.

**The Technic of Diagnosis by Smear** was detailed by Johansen (TexasSJM 35 420 1940): Select the site carefully usually the indurated portion of a lesion or the raised margin of a macule or suspicious infiltration of forehead or face. Cleanse the skin with alcohol, pinch up a fold with compression sufficient to control bleeding, then penetrate the skin superficially with a clean scalpel. Wipe off the first drop of exudation turn the blade transverse to the incision line and scrape the sides and bottom of the cut sufficiently to obtain subepidermal tissue pulp. Smear this material uniformly on a slide and stain with the Ziehl-Neelsen method. Ordinary histologic sections are likely to be fallacious unless acid fast organisms are demonstrated.

THE LEPROMIN TEST, histologically a tuberculoid reaction when positive like the tuberculin test. A bouillon culture of the bacillus is used (Hayashi InternatJLep 1: 31 1933) but the test is unreliable (Pan ADS 46 692, 1942). It often becomes positive in normal persons who are closely associated with lepers, Pardo Castello told us. Where the disease is endemic therefore the antigen is worthless in diagnosis, but is significant in prognosis, being negative in malignant lepromatous types and positive in benign forms (Wade J 135 732, 194 ).

THE HISTAMINE TEST provoking erythematous flare about the site of intradermal injection of 0.1 cc of 1 1,000 histamine phosphate when peripheral innervation is intact, is valuable in diagnosis. Leprosy by damaging neural structure eliminates the normal flare (Pardo Castello and Tiant ADS 47 626, 1943).

**Prognosis**.—Few cases of leprosy recover spontaneously and comparatively few as a result of treatment. The tubercular form of the disease is the gravest, death generally occurring as a result of the direct effect of the malady or from intercurrent disorders in from 7 to 15 years. In the anesthetic variety the patient may survive

for many years. Life may be prolonged by appropriate treatment and proper hygienic measures. Clinical improvement may be considerable without great change in the number of bacteria in the lesions, stated Wade et al. (InternatJLepr 7: 471, 1939) so that relapse is always likely. The diffuse lepromatous type, inconspicuous clinically is hopeless, being associated with progressive weakness, anemia, emaciation, and death after perhaps 8 years (Obermayer: AnnWestM&S 1: 225, 1947)

**Treatment.**—The essential step in prophylaxis has been the segregation of infected individuals. Compulsory segregation is being abandoned in favor of out patient clinics for noninfectious cases and voluntary isolation of infectious ones (Rogers and Muir: Leprosy Bristol, 1946)

The ineffectiveness of chaulmoogra oil and its derivatives was discussed by McCoy (PHRpts 57: 1727 1942). Chaulmoogra oil was the one substance which, while not specific, stood the test of time. Large amounts were required to obtain results, and few individuals tolerated the agent in adequate doses of from 0.3 gm. to 1.0 gm. by mouth daily

Promin a proprietary given intravenously with properties of sulfanilamide, inhibited the progress of many cases in a dosage of 5 gm. per day 6 days a week, reported Faget et al. (PHRpts 58: 1729 1943) Allergic pruritus occurred in a sixth of their patients, and urinary and hematologic changes required watching for. Faget and Pogge (PHRpts 60 1165 1945) claimed improvement in 137 cases of lepromatous and mixed types The drug acted slowly benefit becoming apparent only after 6 or more months of treatment. The more enduring the treatment and the larger the dose tolerated, the better were the effects. While improvement was slow it appeared to be steady and with rare relapses, stated Fite and Gemar (SMJ 39: 277 1946) for bacteriemia seemed to be eliminated, and histologic evidence of healing especially about sweat glands could be demonstrated. See Wharton (LeprosyRev 17 96 1946)

Diasone 0.33 to 1.0 gm. orally per day in adults, induced objective improvement in two third of the patient treated 6 months or more, and none got worse (Faget et al. PHRpts 61: 960 1946) but it was not tolerated by one-fourth of the patients to whom it was given.

Typhoid vaccine or milk has been used as foreign protein with due care. During the period of invasion, shock therapy is contraindicated With foreign protein therapy to exceed the patient's tolerance is to provoke a lepra reaction which is debilitating, liable to spread the disease and may possibly prove fatal. Diphtheria toxoid therapy proved disappointing (Faget and Johansen PHRpts 57: 249 1942) Fever therapy is probably futile (Johansen and Trautman InternatJLepr 365 1939)

Neuritic pain may be relieved in only 1 or days by injecting intramuscularly 300 units of vitamin $B_1$. Lepra reactions may yield to Benadryl.

Radiotherapy is a valuable local agent. Solid carbon dioxide has proved beneficial. The advisability of destroying nodules by curettage or other means is dubious.

Ulcers, contractions and mutilations are to be treated surgically while physiotherapy hydrotherapy and electrotherapy may do much to lessen deformity

## GRANULOMA INGUINALE

**Symptoms.**—Granuloma inguinale starts in the form of a small macule which develops into a papule A small superficial ulcer soon replaces the papule and the disease progresses slowly as a chronic, superficial serpiginous, sclerosing, granulomatous ulceration There is no formation of abscesses at any time It is exceptional for healing to occur spontaneously if it ever does. The ulcers are superficial with somewhat raised, nodular irregular borders. They give rise to comparatively little pain. There is seldom associated lymphadenitis Nodular ulcerovegetative, hypertrophic, and cicatricial types are recognized (Halty's classification Pariser and Beerman AmJMSc 208 547 1944) Pelvic involvement, including fatal cases, was described by Pund and McInnes (Clin 3 221 1944) malaise, weakness, fever anemia, and leucocytosis are features. Polyarticular arthritis and osteomyelitis were noted by Lyford et al (AmJS 28 585, 1944) Extragenital cases are recognized (Greenblatt et al ADS 38 358, 1938) The lip neck, mouth and elsewhere, generally in association

with pudendal lesions, are sites which have been involved. These cases, too, respond to specific treatment (J 116 2406 1941)

**Etiology**—Pund and Greenblatt (APath 23 224, 1937) demonstrated the presence of *true* Donovan bodies in their cases with regularity and dependability both in smears and in sections. Intradermal injection of triturated infected material may yield positive tuberculoid reactions (Kornblith: ADS 50 276 1944) The Donovan body was apparently successfully cultivated in the yolk sac as an encapsulated bacterium named



Fig. 272.—Granuloma inguinale. (Dr C. C. Dennie.)



Fig. 273



Fig. 274.

Fig. 273.—Donovan bodies in large monocytes. (Pund et al APath 23 224, 1937)
Fig. 274.—Donovan bodies, Wright's stain. (Fo J 87 1788, 1926.)

*Donovania granulomatis* by Anderson et al (AmJS 29 165 1945 JExpM 81 25, 1945) See Cornwall and Peck (ADS 12 613 1925) Experimentally reproduced infections in human beings were described by Greenblatt et al. (J 113 1109 1939) Perhaps infection is transmitted by pubic lice (Butts and Olansky ADS 54 524 1946) A yolk sac culture produced a successful human inoculation as reported by Dienst et al. (AmJS 31; 614 1947) The culture used as *antigen* gave positive tuberculoid skin reactions, and positive complement fixation tests were reported by Jennison et al. (ADS 55 324 1947) Of the many chemotherapeutic agents tried, streptomycin in the extremely low concentration of 6.2 gamma per ml. was most effective in protecting the chick embryo (Rake and Dunham

AmJS 31 610 1947) Success in cultivating the organism on an artificial medium of beef heart infusion broth with some normal egg yolk was obtained by Durham and Rake (AmJS 32 145 1948)

**Treatment.**—Excellent results follow the intravenous injection of 5 c.c. of 1 per cent aqueous solution of potassium antimony tartrate on alternate days. The drug is likely to provoke vomiting unless given conservatively. A dose of 5 c.c. of the 1 per cent solution may be increased 1 c.c. at a time to perhaps 10 c.c., intravenously. Antimony treatment must be persisted with until the lesions are healed. Fuadin, a complex trivalent antimony compound, is highly effectual and relatively nontoxic. Better than antimony, however, is streptomycin, which has been found curative by Barton et al (ADS 56 1 1947) and Kupperman et al. (Trans ADA 1947). A dose of 0.5 gm. per 6 hours for 2 weeks may be recommended for a total of less than 4 gm. is likely to be followed by relapse. Donovan bodies cannot be found after the fourteenth day and are often gone by the sixth. The hazards of eighth nerve damage, kidney injury and depression of the bone marrow must be borne in mind when streptomycin is used. Streptomycin 4 gm. per day for 5 days is usually adequate, wrote Greenblatt et al. (JVDI 28 3 1947). Hirsh and Taggart (AmJS 32 109 1948) cured all 21 patients with 0.17 gm. given 6 times a day for from 6 to 47 days. On 4 gm. per day for 5 days, 50 of 51 cases were reported cured by Kupperman et al (J 136 84 1948)

## RAT BITE FEVER

**Symptoms.**—Rat bite may inoculate *Spirillum minus*, the cause of the usual variety of rat bite fever (sodoku), or *Streptobacillus moniliformis*. The disease followed a cat bite in the patient of Swyer (BMJ 2 896, 1945). *S. minus* is a naturally occurring parasite of rats, a short, thick, actively motile organism with tapering ends and one or more flagella. After an incubation period of 10 to 40 days, the original wound having healed, a nonpurulent inflammation recurs at the scar and lymphangitis and symptoms of general infection develop with intermittent fever of 2 to 7-day periodicity. Erythematous indurated plaques develop at the inoculation site and undergo exacerbation with each rise of temperature. A satellite bubo is usual, and spirilla may be found here as well as in the chancre on dark field examination (Chopra et al.: IndMGaz 4 449 1939). Of 63 cases of rat bite treated at the Johns Hopkins Hospital 10 per cent got the disease; 60 per cent were under 1 year of age; and none died (Richter: J 128 324, 1945). Serologic tests for syphilis become positive in this as in other spirochetoses.

**Haverhill Fever (Erythema Arthriticum Epidemicum)**, an illness recognized in Massachusetts in 1926 (Place and Sutton: AIntM 54 659 1934), is characterized by abrupt onset with chills, fever, vomiting, headache, pains in the back, and arthralgia. A macular, papular or petechial rash appears early, especially on the extensor aspect of the extremities. The organism cultivated from the blood was called *Haverhillia multiformis*, later identified as *Streptobacillus moniliformis*. Rat bite inoculated this disease in the case of Farrell et al. (AIntM 64 1 1939). Of 3 cases of rat bite fever of Kirkwood and Still (BMJ 60 141 1941) 2 were spirillar and 1 streptobacillary. In the latter type of infection the incubation period is brief, only 3 to 5 days, the fever falls after only a few days, and the rash is morbilliform. A secondary fever appears soon after the first defervescence, is quickly followed by polyarthritis, and may persist for weeks or months.

**Treatment.**—Neoarsphenamine was effective in the cases of Chopra and of Gilkey and Dean (*BMJ 32 1109 1930*). *It fails in Haverhill fever* but penicillin is great fungly effective (Wheeler: AmJDisChild 69: 215 1945; Altemeier: J 127 270 1945). See Lominski et al. (BMJ 2 510 1949)

## PINTA

Pinta is a common disorder of Mexico and Central America, characterized by startling depigmentary changes. A disease of interesting and exotic history, it was long and erroneously thought mycotic in origin.



Fig. 275.



Fig. 276.

Fig. 275.—Pinta. Hipopigmentation of nose and lips in untreated boy, dark field positive. (Dr Robert Andrade.)

Fig. 276.—Ichthyosiform pinta of leg, in untreated boy, dark field positive. (Dr Robert Andrade.)





Figs. 277 and 278.—Pinta. (Dr Howard Fox.)



Fig. 279

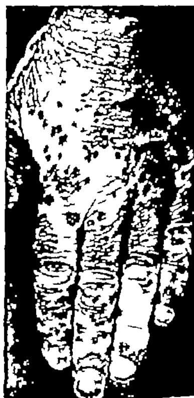


Fig. 280.

Fig. 279.—Pinta. Hand and scrotum lesions. (Pardo-Costello and Ferrer. A.D.S. 45: 842, 1942.)

Fig. 280.—Pinta. (Dr. O. G. Costa.)



Fig. 281.—Pinta, showing superficial location of inflammation suggestive of mild lichenoid dermatitis. (Dr. Edw. A. Gall.)

On Aug. 8, 1938, a treponema was discovered in the serum of scrapings from active lesions by Armenteros and Triana in Saenz's patient in Havana, the organism being demonstrated in lymph nodes and tissues of this patient 3 days later by Leon y Blanco (BerMiler 18: 617, 1938). See valuable review of Holcomb (USNMBull 40: 517 1942) and Edit. (J 126: 1030, 1944)

*T carateum* is a straight spiral 7 to 15 μ in length with 6 to 1 coils, rigid and regular. It occurs in the blue lesions. Leon y Blanco inoculated himself successfully and, with Latapi (Medicina 20: 315 1940, abs ADS 46: 149 1942) described early lesions. They accredited Herrejon with having earlier established the spirochetal nature of the disease (VDI 21: 270 1940)

In the experimental disease, a small lenticular papule develops on the seventh day at the site of inoculation. This reaches maximum development within 3 weeks, becoming a scaly flattened, oval plaque of 2 to 3 cm. diameter which remains solitary for 3 to 9 months. The dissemination of a secondary generalized eruption sets in. The lesions are hamlike or slate colored, superficial and scaly identical with those of naturally acquired pinta, and are accompanied by the development of positive serologic reactions for syphilis.

When *T carateum* was inoculated into each of 9 patients with yaws and free from syphilis, pinta developed in only 2 (Goncalves abs BJD 59: 272, 1947)

The naturally acquired chancre develops in 2 stages (Blanco and Lacosa: AmJS 31 600 1947) at first resembling an infiltrated papule and later becoming an erythematosquamous patch of a size varying with its period of evolution. The lentil size early papule is visible within 10 days or less, becomes an oval, brownish-red plaque within a month, either elevated 2 or 3 mm. or level with a halo of scales. This becomes a flattened, sharply demarcated oval patch, somewhat infiltrated, pinkish, and furfuraceously scaly. If the scales are scraped off, the surface is lichenoid. Slow progression ensues with centrifugal expansion and confluence of peripheral lesions. The late primary lesion may be psoriasiform dermatomycotic in appearance or lichenoid. The initial lesion occurs on the lower extremities in 80 per cent of the cases, on the upper extremities in 10 per cent and on the face in 5 per cent. Dissemination does not occur earlier than 2 months and may be delayed even several years.

Pintids are erythematosquamous plaques like the primary. They appear in crops and do not disappear spontaneously. They remain localized or if generalized, are not as a rule distributed with symmetry. The lesions result in depigmentation. On a dark skin, bluish scaly lesions and sharply defined vitiliginous lesions may coexist. Remarkable variation of color is seen, and dyschromic patches are often checkered. Pruritus with secondary infection may modify the picture.

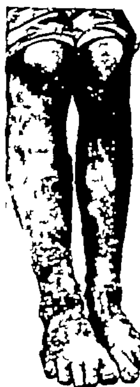
Lymphatic involvement is discrete nontender and syphiloid. Melanotic pigment and curious hyaline corpuscles are found in the nodes (Beerman: AmJMSc 205 611 1943). Serologic tests become positive in all late cases and are likely to be irreversible. Spinal fluid changes like those of syphilis were found in half of the 41 cases studied by Pardo-Castello and Ferrer (ADS 46 843 1942) and cardiovascular changes in two-thirds of them. Neurologic and cardiovascular involvement is fully as significant in pinta as in syphilis. Lieberthal (J 123 619 1942) described cases in the United States with late manifestations.

Treatment of pinta is like that of syphilis. Mapharsen and penicillin are effective, although dyschromia remains, as a rule (Varela and Avila AmJTropM 27 663 1947)

## YAWS

**Yaws (Frambesia)** is infection with a spirochete *Treponema pertenue* which closely resembles the organism of syphilis. Yaws is endemic in certain tropical countries. The course of the disease may be roughly





Figs 282 and 283—Yaws (Dr J A. Johnston.)



Fig 284



Fig 285



Fig 286

Fig 284 Yaws (Dr Isador Dyer )
Fig 285 Yaws resembling gummatous syphilis) (Dr J A Johnston )
Fig 286 Yaws facial destruction or gangosa. (Drs. Musgra and Marshall)

divided into 3 stages a primary stage including the stage of inoculation which varies in duration from 2 to several weeks or longer followed by the appearance of the mother yaw the analogue of the syphilitic chancre a secondary period marked by the appearance 1 to 3 months after the development of the mother yaw of a generalized papular eruption which persists for several weeks or months and ultimately a third stage in which gummatous nodules and ulcers occur

Striking features of yaws (Fox J 123 409 1943) are the normally extragenital manner of inoculation, the keratotic lesions of the soles, the absence of mucosal lesions in the early stages, the infrequency with which a secondary eruption is seen, and the clinical identity of late manifestations with those of syphilis.

Some 70 per cent of the cases occur in children under 10 years of age Castellani s *T pertenue* infects almost exclusively Negroes in equatorial Africa In the Pacific islands including the Philippines, Malay States, Burma, and Thailand, and also in Haiti Santo Domingo, Jamaica, and parts of South America.





Fig. 287 Fig. 288. Fig. 289

Fig. 287.—Yaws. Corymbose, papulosquamous eruption. (Dr O G Costa.)
Fig. 288.—Yaws Leukoderma (Dr O. G. Costa.)
Fig. 289.—Yaws. Psoriasiform lesions in pot-bellied child. (Dr O G Costa )

The initial lesion often occurs on the leg, perhaps inoculated by flies The mother yaw when it is seen is of the same type as the common frambesiform eruption excepting its larger size.

The typical secondary eruption when seen, more resembles impetigo than any manifestation of syphilis. Volar hyperkeratotic lesions of yaws seen often in the West Indies may result in a crablike gait. Lesions resembling lichen scrofulosus are sometimes observed. Pigmentary changes like those in pinta are found.

While spinal fluid changes were demonstrated in half the cases examined no symptoms of neurologic involvement were reported by Pardo Castello (ADS 40 762, 1939) in a valuable study of 500 cases in Cuba. Iritis does not occur

Juxta articular nodes may reach the size of an orange in a decade or more of persistence and slow growth (Chambers ADS 30 103, 1944)

Osseous involvement is common with more rapid and painful manifestations than occur in syphilis (Helfet JB&JSurg 26 672, 1944) Marked x ray changes develop in only a few weeks, perhaps simulating osteomyelitis following trauma and accompanied by fever swelling, and muscle spasm. Sites of predilection are the tibial,

distal femoral, medial clavicular and distal humerus regions. Osseous as well as other manifestations are dramatically responsive to antisyphilitic chemotherapy

Penicillin is effective (Whitehill and Austrian BullUSAMD 1946, p 84 Hill et al. Lancet 2 622, 1946 Dwindelle et al. AmJTropM 26 311 1946 27 633 1947) Relapses occur as in syphilis. The Wassermann test is positive as in syphilis. Yaws is as hard to cure as syphilis, and it is treated in the same way

## BEJEL

Bejel.—Syphilis among the Bedouins is called *bejel*. Hudson (ADS 33: 994 1936) described this interesting community infection, which, among the isolated peoples of the Middle Euphrates Valley, is contracted nonvenereally in childhood in the majority of instances. The epidemiology of bejel is comparable with that of yaws. The response to bismuth therapy is favorable. This mild type of spirochetosis is thought to be due to a mild strain of the organism. The public health and economic aspects of it were studied by Hudson and Crosley (JTropM Sept. 2, 1936, p. 240) According to Hasselmann (ADS 38: 837 1939), the exclusive transmission of syphilis among Arabs by nonsexual means is a myth. Hasselmann considered *bejel* simply one of many colloquial names for syphilis, all these names being indiscriminately used for all cutaneous ulcers. Syphilitic abortion is commonplace. The disease is not yaws. It is misleading and confusing to call [syphilis] by different, local colloquial names, for it runs the same course [among the Arabs] as elsewhere. Syphilis, yaws, pinta, and bejel were interpreted as various modification mainly on climatologic grounds, of one disease by Hudson (*Treponematosis*, Oxford Univ Press, 1946)

Witkop (Dikwakwadi, White Head ) is a favoid condition of the scalp, characterized by the formation of white, hard, dry superficially friable confluent, firmly adherent crusts, which give the appearance of a tightly fitting white skull cap. The disease is chronic and slow in evolution. It is seen only among syphilitic natives of South Africa, being most prevalent in British Bechuanaland where almost the entire native population is syphilitic. See Fraser (BJD 34: 267 1922)

## SYPHILIS

Syphilis is an infectious disease due to *Spirochaeta pallida* (*Treponema pallidum*) of great chronicity systemic from the outset, capable of involving practically every structure in the body in its course and of simulating a large proportion of the entities comprising the field of medicine and the specialties, distinguished by florid manifestations on the one hand and years of asymptomatic latency on the other transmissible to offspring in man, transmissible to certain laboratory animals, and specifically treatable to the point of presumptive—but not thus far demonstrable—cure by the use of penicillin, derivatives of arsenic, mercury and bismuth and fever therapy (Stokes et al. Modern Clinical Syphilology Saunders, 1944)

Syphilis is widespread among the populations of every country In the United States of America it was generously estimated that 500 000 new infections were contracted during 1935 and that the cost to the Nation annually approximated half a billion dollars. The incidence in 2 million draftees approximated 4 per cent in the white and 20 per cent in the Negro (Vonerlehr and Usilton J 120 1369 1942) It is likely to cost taxpayers a great deal more (Stokes et al AmJMSc 199 586 1940) The history of syphilis was briefly and interestingly outlined by Kemp (AmJS 24 759 1940)

## ACQUIRED SYPHILIS

**Outline of Course and Pathologic Background of Syphilis.**—A primary incubation period follows inoculation. Although there are no

clinical signs of infection during this time, reproduction of spirochetes progresses rapidly in perivascular tissues with general hematogenous dissemination in a very short time. The primary stage is marked by the appearance of the chancre with wide variability in the local reaction. There is satellite lymphadenitis, and systemic symptoms may be manifest such as headache, bone pains, lassitude, and malaise. The chancre is produced by lymphocytic and plasma cell infiltration to form a papule at the site of inoculation. Reproduction of organisms here is at its height. Other foci of similar inflammatory structure are developing throughout the body their number, location and activity dependent on the virulence of the organism and the peculiarities of the host. Spirochetal septicemia is present. Serologic alterations begin which result in a positive reaction to tests.

The chancre begins to heal in the early secondary stage, and disseminated manifestations develop with lymphadenitis, skin lesions, enlargement of the spleen, and osseous, cerebrospinal, hepatic, and nephritic lesions. Serologic reaction is now positive. Local immune reactions begin to destroy spirochetes in the chancre and elsewhere, and healing sets in. Enormous numbers of new foci are established in the skin, bones, lymphatics, and viscera. Lymphocytes disappear from the healing foci and fibrosis occurs. The organisms are partially destroyed or suppressed. Activity declines throughout most of the body but innumerable foci remain in the perivascular lymphatics and lymph nodes.

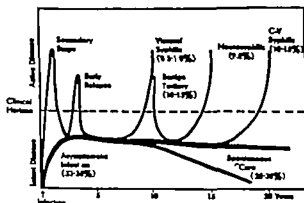



Fig. 290 —The possible courses of syphilitic infection, diagrammatic. (Morgan J 113 211, 1939 )

Late in the secondary stage the eruption tends to disappear spontaneously and systemic manifestations subside coincidentally with widespread destruction of spirochetes. A few remain and provide the basis for relapse. The blood stream contains few of them.

With defects of local resistance and revival of foci, occasional showers of spirochetes and crops of lesions may reappear especially on mucous surfaces. The primary lesion and secondary eruption may recur if they had been temporarily aborted by inadequate treatment.

Latency may be established after a time in the prolonged absence of symptoms, or relative quiescence may be punctuated by occasional relapses. Spirochetes are few in number and are held in suppression by systemic and local defense mechanisms. Local lesions, especially of the

mucosae bones, and skin, may flare. Chronic inflammatory defense is active but inconspicuous. It results in degenerative changes and fibrosis. The fetus of a syphilitic woman is likely to be infected.

Latency may persist for many years, but a late phase is likely to appear. Its characteristic lesion is the gumma. Gummas are tumorlike masses of granulomatous structure which appear in various organs, skin, liver, bones and brain. Endarteritis produces ischemia and necrosis, sloughing destruction, and scarring. These lesions are comparatively noninfectious, and are apparently due to massive tissue reaction (allergic?) to a small number of organisms.

Degenerative lesions of the cardiovascular and nervous systems and fibrosis of parenchymatous organs, such as liver, spleen and pancreas, occur in late stages. Spirochetes are present and may be numerous, but are usually demonstrable only on special search in microscopic foci in the aorta, heart muscle, meninges, and viscera. Serologic reaction may have become negative.

**The Chancre,** the primary lesion of acquired syphilis, develops at the point of inoculation, usually within 2 to 6 weeks. It generally is a small, firm inflammatory infiltration which becomes eroded and from which oozes a stringy nonpurulent exudate. Spirochetes can be found on dark field examination of the exudate. Extragenital chancres are more ulcerative than the usual ones at the coronal sulcus (Wile and Holman AmJS 25 58 1941). As a rule chancres are single but they may be multiple. A chancre may be mixed with chancroidal infection. The lesion may occur anywhere. Sites of predilection are glans, corona, and shaft of penis, and external uterine os in the female. The intraurethral location is not exceptional, induration being palpable as a rule if it is sought, the diagnosis confirmed by dark field examination of material aspirated from the satellite inguinal nodes (Loveman and Morrow AmJS 28 49 1944). Frequent extragenital locations are lips, mouth and hands, especially of physicians and nurses (Downing ADS 39 150 1939). We have seen a woman with chancres on both nipples. Extragenital chancres are often unrecognized, yet any indolent indurated lesion anywhere on the body, especially if accompanied by unilateral adenopathy, should arouse suspicion of syphilis (Tucker et al AmJS 32 345 1948) and can generally be identified by dark field examination. Infection has been acquired from blood transfusion without a primary sore (Fichenlaub and Stolar PaMJ 42 1437 1939). The tonsillar primary sore is accompanied by cervical adenitis capable of being mistaken for Hodgkin's disease. When gonorrhea and syphilis are coincidentally acquired, the former may mask the latter, particularly when penicillin is used, so that syphilis is partially aborted only to appear later; the gonorrheal patient treated with penicillin must be followed for several months (Leifer and Martin J 130 202 1946).

Acquired syphilis is not limited in its incidence to adolescents and adults; chancre of the umbilicus of the newborn has been observed, and children have been infected innocently (Creswell et al AmJDisChild 66 611 1943).

**Mixed Chancres** are lesions infected with both *Spirochaeta pallida* and *H ducreyi*. They are characterized by a markedly inflammatory aspect, a tendency to ulcerate extensively, and early chancroidal involvement of associated lymph nodes. Chancroidal symptoms so overshadow syphilitic



Fig. 291.



Fig. 292.

Fig. 291.—Syphilitic chancre seronegative primary

Fig. 292.—Chancre of cervix, the common but obscure primary sore in the female. (Drs Stokey and Scarpellino.)



Fig. 293



Fig. 294

Fig 293—Syphilitic chancre (Drs. Fordyce and McKee.)

Fig. 294.—Primary syphilitic sore of the tongue. (Dr Grover Wende.)



Fig 295.



Fig. 296.



Fig. 297

Fig 295—Syphilitic chancre (Dr Fordyce and McKee.)

Fig. 296.—Primary syphilitic paronychia (Dr H E Michelson.)

Fig. 297—Chancre of cheek, following bite (Dr Philip Shaffner.)

that diagnosis may be seriously confused, even until the appearance of a secondary eruption or a positive serologic reaction.

DIAGNOSIS OF THE CHANCRE.—Clinical characters are not pathognomonic, and only positive dark field examination is reliable. The relatively indolent nature of the syphilitic lesion, the long period of incubation, the induration, and the lack of response to local medication are typical features. One should select for dark field study lesions which are as young as possible, as nearly untreated as possible, and as clean and free from detritus and secondary infection as possible (Cares: JLCM 29 12, 1944) Treatment must be deferred until diagnosis is indisputable

The chancre rarely may persist for a long time in spite of treatment.

**Mucocutaneous Relapse** occurred in 6 per cent of some 6 000 patients of a Cooperative Group survey and is seen mainly in early cases and shortly after the cessation of treatment. One form of relapse is the recurrence of the chancre, the lesion duplicating the primary The commonest lesion of infectious relapse is the mucous patch papular lesions, moist or dry are also common (Pariser J 113 1206 1939)

PSEUDOCHANCRE REDUX is a late, gummatous, syphilitic inflammation appearing at the site of the chancre, but the satellite adenitis of a primary sore is lacking

**Reinfection** after cure can and often does occur (Cannon AmJS 17 459 1933 Schoch and Alexander ib 27 15 1943) Reinfection comprise a high but difficultly determined proportion of what must be reported as relapses in evaluation studies of treatment methods.

**Second Incubation Period.**—Following the appearance of the chancre there is usually a second comparatively quiescent period of several weeks. Vague joint pains, headache, slight fever malaise and loss of weight are usual accompaniments. Such symptoms may be mild or severe, and they accompany as well as precede the secondary eruption.

**Lymph Node Involvement.**—The satellite bubo which drains the chancre site and appears early is firm painless, freely movable, *fusiform*, olive-sized, and typical It does not suppurate unless the infection is a mixed one. It may be unilateral or bilateral, and it is not necessarily on the same side of the body as the primary sore contralateral adenitis usually means syphilis (Fowler BJD 60 279 1948) It is of especial diagnostic importance in extragenital chancres Herpes simplex also is associated with a satellite gland, but this is large, painful, and evanescent.

Immediately after infection takes place spirochetes begin to multiply and invade surrounding tissues, gaining access to lymphatics and blood stream and are widely distributed over the body even before the initial lesion can be detected Lymph nodes become palpable early in the course of the disease between the fifth day and the tenth They are smooth, firm oval pea to nut sized, elastic subcutaneous masses, which are painless and freely movable never fluctuant or matted together Enlargement of epitrochlear occipital and posterior cervical nodes is of greatest import (Beeson ADS 32 746, 1935) Too much diagnostic value should not be placed on the presence of palpable lymph nodes, however (Martin Lancet 1 363 1947) They are palpably enlarged in some 70 per cent of early cases. Lymphadenitis in late syphilis is common though frequently unrecognized and is responsive to appropriate treatment. Fluid obtained from lymph nodes in early syphilis often contains demonstrable spirochetes (Loveman and Morrow AmJS 28 44 1944)

**Syphilids** are the cutaneous manifestations of syphilitic infection. The eruptions of acquired syphilis were classified by Fox (JCutDis 31 224 1913):

| Early | Late |
|---|---|
| Macular | Nodular |
| Maculopapular | Squamous |
| Papular | Gummatous |
| Papulopustular | |
| Pustular | |

Cutaneous manifestations of syphilis show great variability in character and in appearance. Lesions may be sparse or diffuse. They are generally multiform, discrete and comparatively painless, and are never vesicular. Because of their multiformity and range of distribution the lesions may simulate those of many other dermatoses. Syphilids possess certain peculiarities which when considered collectively usually suffice to render clinical recognition possible. They generally develop slowly and in successive crops, which, owing to the tardy disappearance of the preceding lesions, tend to overlap. During the exanthematous stage the distribution of the lesions is more or less symmetric, but later especially in relapsing cases, the eruption is often scanty and may involve only certain small areas, favored sites being the nasolabial folds, the palms, and the upper margin of the forehead. In late stages, the lesions tend to appear in groups, and serpiginous and arcuate forms are common. They are usually reddish, brownish red or coppery in color. Accompanying symptoms often include lymph node involvement, cephalalgia, laryngitis and pharyngitis, and eroded papules or mucous plaques in the mouth and other orifices. In the *scalp early syphilis may give rise to patchy moth-eaten alopecia.* Gummatous lesions of the scalp cause cicatrization and permanent alopecia. The nails may be affected at any stage of the disease. The forefinger is a likely extragenital site for the chancre. Late syphilids may occur in the nail bed, with deformity of the plate. Inflammatory or ulcerative paronychia may result.

**Macular Syphilid.**—This is the earliest of the so-called secondary manifestations. It corresponds to symptomatic roseolas of other infections. The eruption is general and symmetric, and usually appears within 3 to 6 weeks after the chancre. The lesions are fairly uniform discrete, erythematous, oval macules. They range from 0.5 to 2 cm. in diameter. The sites of predilection are the abdomen, sides of the trunk, arms, and palms and soles, although no region is exempt. The roseola may be more readily seen at a distance than when close to the examiner. It gives rise to no symptoms. It may disappear spontaneously. Occasionally it is followed by slight, temporary pigmentation. Recurrences are rarely noted, the lesions being scanty in number segmented or circinate in outline, and located usually on the forearms, thighs, and buttocks. If the disease has not been recognized, treated, and so caused to recede, or if it does not recede because of the autochthonous development of immunity the macules instead of disappearing may undergo further proliferative changes so that macules, maculopapules, papules, and pustules coexist.

**Vitiligoid and Pigmentary Syphilids.**—Melanotic hyperpigmentation of the skin occurs in and near syphilitic lesions, especially when they heal. Vitiligoid depigmentation occurs usually on the back and sides of the neck, consisting of oval ill-defined, asymptomatic pigment free patches,



Fig. 301.



Fig. 302.

Fig. 301.—Secondary papulosquamous syphilid.
Fig. 302.—Follicular maculopapular syphilid. (Dr. L. W. Ketron.)



Fig. 303.—Corneous syphilid of volar skin. (Dr. C. C. Dennie.)



Fig. 304.



Fig. 305.

Fig. 304.—Mucous patches. (Dr Sweitzer.)
Fig. 305.—Moist papular syphilid, perianal.



Fig. 306.



Fig. 307



Fig. 308.

Fig. 306.—"Split papules. (Dr Michelson.)
Fig. 307.—Annular secondary syphilid. (Dr Ketron.)
Fig. 308.—Condyloma latum. (Drs. Fordyce and MacKee.)

**Syphilids of the Palms and Soles** are usually dry in both the secondary and tertiary stages of the disease. Owing to the density of the corneum, the appearance of the lesions is considerably modified. Macular eruptions of the palms and soles occur as part of the general roseola, *but papular and nodular forms may be more or less limited to volar regions*, especially in relapsing cases. Symptoms are usually absent aside from inflexibility but painful fissures may develop. Macerated with sweat, syphilids about the toes can resemble tinea.

**Atrophy** may follow the lesions of secondary syphilis, just as it characterizes the scarring of late lesions. It manifests itself in soft, atrophic macules which may be elevated or depressed, in the distribution of the eruption on which their existence depends (see macular atrophy). Destruction of elastic tissue by the pathologic process is the cause of the lesion, and syphilis is not the only cause (Scull and Nomland: ADS 36 809 1937).

**Pustular Syphilids** may be separated into groups.

SMALL ACUMINATE PUSTULAR SYPHILID.—*The lesions are generally* follicular and tiny and they are likely to be seen along with ordinary acuminate papular syphilids. The pustules are discrete, conic, numerous, and symmetrically distributed over the trunk and extremities. They commonly occur during relapses, especially in cases insufficiently treated. On disappearing they generally leave temporary stains and occasionally small scars.

LARGE ACUMINATE PUSTULAR SYPHILID.—The lesions, sometimes termed the acneform syphilid, are pea size or larger discrete, acuminate pustules which are located at the follicular orifices and generally involve the face, trunk and limbs. Occasionally the eruption strikingly resembles smallpox and is called a varioliform syphilid. The lesions usually develop slowly and in crops. They may be grouped, but as a rule they are scantily distributed over the whole body being most profuse on the face.

FLAT PUSTULAR SYPHILID.—Lesions of this variety impetiginoid and ecthymiform syphilids, are flat pea to dime size, yellowish or brownish, superficial pustules. On the scalp trunk and extremities, the eruption is usually scattered but predilection is noted for the face and the genital and anal regions. Large acuminate papules and large, flat pustules may be present along with macular elements. The crusts are oval or irregular in outline and of various thicknesses. Underlying ulcers are superficial and only slightly inflamed or less commonly deep and crateriform with purplish congested areolae. Confluence of lesions may give rise to the formation of extensive crusts. Crusting and ulceration may be conspicuous in early malignant syphilis, constituting the rupial syphilid (*Thetford* and *Callaway*: UCutRev 44 306 1940).

PUSTULO-ULCERATIVE SYPHILID.—The destructive factor is pronounced, and the lesions are brownish or purplish in color with infiltrated bases and thick crusts overlying seropurulent exudate.

**Diagnostic Features of Secondary Syphilitic Eruptions** are

*Multiplicity of lesions.*
*Widespread distribution, even if the lesions are few.*
*Discreteness.*
*Polymorphism, macules, papules, pustules, ulcers, and scaling lesions being present simultaneously.*

Tendency to form circular, annular oval, or reniform lesions, and to group in crescentic, serpiginous, or corymbiform arrangements.
Absence of itching, except in follicular eruptions, which itch.
Absence of pain, except in digital and infected ulcers.
Involvement of the mucosae and sore throat.
Generalized lymphadenopathy in which the nodes are painless, small and discrete.
Constitutional manifestations which include malaise, anorexia, fever headache deep aching pains, and loss of weight.
Positive serologic reaction.

**Tubercular or Nodular Syphilid** occurs late in the course of the disease, seldom before the end of the first year and usually in the third or fourth. From both clinical and histologic standpoints, it is gumma of the skin. Lesions range from pinhead to large pea size They are limited in number and are seldom of general distribution. Sites of predilection are the face, especially the forehead, scapular and interscapular regions and extremities. Syphilids of this variety exhibit a strong tendency to form groups and to coalesce with the formation of arcuate, reniform and serpiginous patches.

Syphilitic tubercles are smooth rounded, circumscribed elevations, reddish or brownish in color and firm in consistency developing slowly and persisting for weeks or months. Tubercles may disappear with or without ulceration, but there is always scarring The cicatrices in the absence of ulceration are rounded, atrophic and of mottled hyperpigmentation and depigmentation. In ulcerative cases they are thin, glazed and parchmentlike, occasionally with some scaling New lesions spring up at the borders of the plaques, and may undergo regression only to be replaced marginally by fresh ones. So areas of large extent may be affected in the course of years.

**Gummatous Syphilid.**—In malignant syphilis, gummatous lesions may develop early in the disease, but as a rule they do not occur before the second year Gummas are single or multiple firm, rounded, infiltrated granulomas which involve epidermis only secondarily They are seen as reddish, bluish, or brownish, pea to walnut size or larger circumscribed, oval tumors, which may undergo absorption but generally ulcerate with the formation of soft, sharply defined, punched-out, notably painless sores. The ulcers are reddish or purplish in color with flabby necrotic edges and red, sometimes greenish, granular floors bathed with mucinous pus. They may involve only the dermis and epidermis, but subcutaneous tissues are generally attacked.

While gummas are here described as they appear in the skin, they may affect any organ of the body such as the brain, where their presence causes symptoms of tumor In the breast the lesion simulates carcinoma (Braunstein and Woolsey AmJS 24 43 1940) Their location determines their symptoms. Trauma is likely to influence their location (Higoumenakis abs AmJS 24 662, 1940)

Gummas are commonly single but may be multiple. The usual sites are the thighs, buttocks, calves, forehead, and scalp No region is exempt. Ulcerative destruction and disfigurement are great, especially if the face is involved. Following an injury to a syphilitic individual, the granulomatous syphilid may develop instead of physiologic inflammation and healing. Diseases as well as injuries serve to localize syphilitic inflammation, and seborrheic dermatitis may promote the localization of superficial syphilids.



Fig. 317



Fig. 318.

Fig. 317.—Gummatous syphilid.
Fig. 318.—Syphilitic gumma of tongue. (Dr. George M. MacKee.)



Fig. 319



Fig. 320.

Fig. 319.—Syphilitic gumma, buttock.
Fig. 320.—Gummatous destruction of face. (Dr. J. W. Perkins.)



Fig. 121.—Gummatous syphilid of thigh and leg. (Dr Royal M. Montgomery.)



Fig. 122.



Fig. 123.

Fig. 122.—Zosiform distribution of late syphilid on the back. (Dr Clyde Cummer.)
Fig. 123.—Ulcerated gumma of the leg.



Fig. 124.



Fig. 125.

Fig. 124.—Serpiginous ulcerative syphilid of the nucha and back. (Dr [illegible])
Fig. 125.—Gummatous syphilid. (Dr O. G. Costa.)

**Precocious Gumma.**—In malignant precocious syphilis, gummas may develop within a few weeks instead of months or years after infection.

**Juxta Articular Nodes,** or fibroid gummas, are rounded or polylobed, firm, painless lesions occurring within or beneath the skin in the region of the joints (Greenbaum and Cobane AmJS 18: 289, 1934) They occur in late syphilis, resemble xanthomas, are associated with positive serologic tests and respond to antisyphilitic therapy (Hopkins: BullJHH 49: 5 1931; Sweitzer and Winer: ADS 45: 315, 194[?] Kalz and Newton ib. 48: 627 1943)

**Deformed Types of Syphilis** are those in which inadequate treatment has altered to some extent the expected course of the disease. One must treat *seronegative primary cases adequately for with abortive treatment these cases relapse within 90 to 190 days.* Early tertiary syphilis after inadequate treatment is likely to result in serious destructive lesions. When gonorrhea is treated with penicillin and syphilis is coincidentally inoculated with gonorrhea, syphilis is obscured and may later appear in deformed manifestations (Halley: ADS 50: 269 1944) Syphilis so masked may be detected by following the patient with monthly serologic tests for 3 months (Leifer and Martin J 130 "0", 1946) The lesions of scabies may obscure the diagnosis, its lesions influencing the distribution and appearance of the secondary eruption (Rattner J 131 1241 1946)

**Etiology**—Syphilis is due to *Spirochaeta pallida* (*Treponema pallidum*) of Schaudinn and Hoffmann (Arbeit. aus d. k. Gesundheitsamte 22 527 1905) Infection may be acquired by direct or indirect inoculation or through the placenta. Infection usually occurs as a result of direct inoculation generally during coitus. Extragenital infection is common (Rowntree and Hendon J 115 117 1940) Occasionally one infected person may unknowingly or carelessly infect several innocent individuals (Zimmermann AmJS 23 104 1939) Moist lesions of all kinds in syphilis are especially dangerous, a fact which must be made known to every syphilitic and his contacts. The organisms are most numerous in the primary and secondary stages of the disease.

*Lesions of the secondary eruption are fairly readily demonstrated* to be dark field positive (Agee NOrlMSJ 95 329, 1943) An incidence of about 23 per cent of infection of marital partners was noted by O'Leary (PSMMC 15: 1 1940) in a study of the spouses of patients whose treatment had been thought adequate as well as of those whose treatment was inadequate. The fresher the syphilis of the partner the greater the liability to infection of the spouse, but even 5 years was not enough to render this liability a small one, although 10 years sufficed. The blood and lymph are infectious, but the physiologic secretions are not, according to Parker (JInvD 3: 375, 1940) Menstrual blood is infectious, and the vagina is therefore periodically hazardous. Sores in the mouth make saliva infectious when it is (Barnett and Kalcher: JInvD 1 327 1939) A filter passing, dark-field negative inoculum successfully infected rabbits with the Nichols strain of *S. pallida* in the experiments of Wile (AmJS 31 109 1947)

Infectiousness of untreated syphilis gradually diminishes, or immunity increases, until after 4 or 5 years there is considerably less danger of direct transmission; inoculation from gummas has been noted, however The danger of the transmission of syphilis by blood transfusion is a real one (Burke: BMJ 2: 247 1939) The donor may have seronegative primary syphilis, o he may be serologically negative despite his old infection. Spirochetes are not found in the fetus before the fifth month.

*S pallida* is a delicate cylindrical, spiral, motile organism from 4 to 14 microns in length. The number of spirals is from 6 to 16. The organism is anaerobic, and is pathogenic to rabbits, anthropoid apes, monkeys and other animals as well as man. Its presence in the tissue fluid of the active primary or secondary lesion can usually be demonstrated by means of dark field illumination. Some staining methods may be equally useful (Krajian AmJS 23 617 1939) The similarity of *S. pallida*, *T. pertenuis of yaws and T carateum of pinta is notable. Studies of the morphology of* the organism in the tissues by Steiner (APath 29 189 1940) are interesting. The end knob and flagella were demonstrated by electron micrographs by Wile and Kearney (J 122: 167 194 )

The organism at first penetrates and multiplies in the mucous layer of the epidermis and lymph spaces of the corium, but diffusion of the spirochetes throughout

the body is largely by means of the blood stream. The organism dies within a few minutes when dried, but it may remain virulent for days in refrigerated tissues.

Inoculations of 1 to 6 spirochetes into rabbits by Thomas and Morgan (JExpM 59: 297 1934) using single cell technic failed to transmit the infection. The virulence of *S. pallida* in culture is not great. Considerable variations in biologic characters and virulence of strains of spirochetes are recognized. Vaccine does not alter the immunobiologic apparatus sufficiently to engender riddance of spirochetes from the body. Beck (JPathBact 44: 399, 1937) confirmed the failure of many investigations to demonstrate protective antibodies against the spirochete. Immunity is tissue immunity not humoral (Urbach and Beerman: AmJS 31: 102, 104.) Acquired immunity, which can develop only slowly, is responsible for clinical latency, but this immunity is not dependable if unaided by modern therapy, and it is inadequate to protect against reinfection or superinfection (Kolmer: AmJS 22: 426 1938). Recurrence following inadequate treatment of early infections may be more severe than the original reaction to the spirochetes.

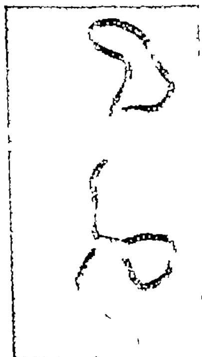


Fig. 216.

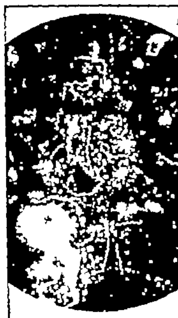


Fig. 217.

Fig. 216.—*S. pallida* ×13,000 electron micrographs. (T. F. Anderson and J. Hillier, RCA Laboratory, Princeton, N. J.)

Fig. 217.—*S. pallida*, dark field illumination. (McCarthy: *Histopathology of Skin Diseases*, Mosby Co.)

The antibody (reagin) in the complement fixation reaction is apparently identical with whatever substance yields the positive flocculation reaction. In the human being it is a product of infection with the spirochete of syphilis, and also it may be produced by the existence of leprosy, malaria, and other infections. Quantitative studies show that the titer of reagin is rapidly reduced by effective antisyphilitic therapy (Belding: AmJS 24: 29, 1940). The syphilitic antigen is associated

with gamma globulins, the separation and purification of which have been studied with great care and with hope of distinguishing the substances responsible for true and falsely positive serologic reactions by Neurath et al. (AmJS 31 347ff 1947) See serologic tests, below

Syphilis seems to be a milder disease in women than in men.



Fig. 328.



Fig. 329.

Fig. 328.—Syphilitic inflammation, acute. Chancre, showing characteristic perivascular lymphocytic infiltration (Drs. Fordyce and MacKee, from Hazen *Syphilis, Its Diagnosis and Treatment* Mosby Co., 1928.)

Fig. 329.—Syphilitic inflammation, tertiary tissue lesion. Lymphocytic and plasma cell infiltration forming collaret about small vessel. (Drs. Fordyce and MacKee, from Hazen *Syphilis*.)



Fig. 330.—Syphilitic inflammation, chronic. Nodular syphilid without ulceration, showing giant cells in granulation tissue. (Drs. Fordyce and MacKee from Hazen *Syphilis*.)

**Pathology**—The microscopic lesion is characterized by perivascular round-cell infiltration (Warthin AmJS 2 425 1918) Minute vessels are the ones mainly involved. The infiltrate in the early stage is made up almost entirely of lymphocytes with a sprinkling of plasma cells. Granulomatous endothelial and fibroblastic proliferation occurs later and more or less giant cell formation is evidenced The infiltrative clumps of round cells, with capillaries at their centers, may coalesce and form what appears to be a massive cellular infiltrate They may cause vascular obstruction and produce necrosis. Nodules are composed of gross masses of infiltration and ulcers result from inflammatory infarction and necrosis of tissue Gummas have the same basic pathology as other syphilitic lesions. A scar results whether absorption occurs or the weakened overlying epidermis sloughs away Spirochetes are few in late syphilitic lesions in contrast with their profusion early in the infection. The reliability of Warthin's criteria for the histologic diagnosis of syphilis was impugned by Rosahn and Schaffer (AmJS 28 27 142, 1944) whose autopsy material was correlated with clinical records and serologic tests, and indicated that Warthin's lesions were related more accurately to the age of the patient than to proved existence of the disease and that syphilis was not very often the cause of shortened life span

**Diagnosis.**—Emphasis must be placed on the necessity for careful consideration of the entire symptom-complex in every suspected case Dependence on the laboratory for diagnostic aid has grown beyond reasonable bounds. Positive or negative serologic reports in the absence of corroborative clinical evidence may be void of practical meaning or even false but persistently positive tests over a period of several months justify the administration of treatment and repeatedly positive tests with rising titer make the diagnosis reasonably secure It is a diagnosis to be made discreetly advisedly and soberly for the consequences to the patient are great. A careful case history and a thorough physical examination of the patient must invariably be made In early stages, the spirochete can usually be found in material from the lesions or satellite nodes. The evolution of the disease occurrence of mucosal lesions, involvement of the lymph nodes, and features of the eruption should attract attention. During the tertiary period cutaneous lesions are generally readily recognizable.

In planning treatment the history of previous treatment and response to it in detail are especially significant The occurrence of repeated miscarriages without apparent cause is suggestive of syphilis in women.

The spinal fluid must be examined the fundamental data including the cell count and its differential constituents, a qualitative test for globulin, total protein quantitatively and colloidal gold or mastic test and a titrated complement fixation test must be made Without spinal fluid study the diagnosis of latency cannot be made The one abnormality diagnostic of syphilis in the spinal fluid is the positive complement fixation test other diseases are capable of altering any or all of the other aspects of the spinal fluid as syphilis does, but falsely positive specific tests are extremely uncommon Base line studies of the nervous system include evaluation of the psyche and tests of the function of cranial nerves including examination of the visual fields and ocular fundi of the response of the pupils in light and accommodation of speech of muscle stretch reflexes particularly at the heels and knees, and of vibratory and pressure sensibility especially of the feet and heels

The blood pressure should be recorded bilaterally and the state of the heart and aorta requires painstaking clinical and roentgenologic investigation, preferably fluoroscopic.

**Serologic Tests** for syphilis depend on detection and preferably quantitative measurement of *reagin*, as the syphilitic antibody is called. Precipitation and complement fixation tests are used (Eagle: Laboratory Diagnosis of Syphilis, Mosby 1937). The precipitation tests entail bringing suspected serum into contact with specially prepared antigen under suitable conditions, whereupon flocculation occurs and is visible if the serum is syphilitic. The complement fixation (Wassermann) tests entail two steps: (1) suspected serum is relieved of its complement by heating and is mixed with specially prepared antigen, then a known quantity of complement is added with the result that complement is used, fixed, if the serum is syphilitic and is not fixed if it is not syphilitic; (2) the fixation or nonfixation of complement is determined by the result of reaction between (1) and a hemolytic indicator composed of sheep red blood cells and heated anti-sheep-cell rabbit serum. If complement was fixed in (1) hemolysis will not occur on the addition of (2), and the test is read as positive, i.e., indicative of the presence of syphilitic antibody in the suspected serum.

Tests must be performed skillfully under standard conditions (Parran et al. J 109: 4-5 1937 see also Serodiagnosis of Syphilis, VDI Suppl. 9, 1939 Parts I and II). A standard test is continually being sought (Kline AmJClPath 18 185 1948).

Results of tests must be interpreted skillfully (Hinrichsen: VDI Suppl. 14, 1941). *Falsely negative and falsely positive reactions sometimes occur* (Kahn: AD8 39 9 1939). The existence of a positive reaction is *not* positive proof that syphilitic infection exists or that existent syphilis must be treated. The existence of a negative reaction is *not* proof that syphilis is not present, or that treatment is not necessary.

SERODIAGNOSIS OF SYPHILIS (By Charles R. Rein)

Serodiagnosis of syphilis was inaugurated by Wassermann, Neisser and Bruck (1906) with their complement fixation test. Soon after Michaelis, using a similar antigen, *the saline extract of syphilitic liver outlined a method for producing visible* precipitates with syphilitic serum, thus describing the first precipitation reaction. This was followed by the discovery that extracts of tissues not containing *Treponema pallidum* are satisfactory antigens for complement fixation and precipitation tests, and that alcoholic extracts of organs from normal animals make more satisfactory antigens than aqueous extracts of syphilitic organs as used previously. These alcoholic extracts of normal tissue are the lipoid fractions. They may be obtained from beef, horse, guinea pig, rabbit, pig, and human tissues. The heart, liver, brain, and muscle are particularly rich in active lipoid substance. Even though these lipoid extracts are not true antigens in the biologic sense, they do react in an extraordinarily specific manner with syphilitic serum. There are numbers of hypotheses regarding the nature of syphilitic reagins and the mechanism of nonspecific lipoid antigen in producing positive serologic reactions for syphilis. As yet, none of the proposed theories fits all facts.

Many modified methods of complement fixation testing were described and accepted, but it was not until about 1923 that the great possibilities of flocculation methods were demonstrated. The chief advantages of the first flocculation tests were their apparent simplicity. Their economy in regard to glassware, reagents, and expenditure of time prompted their use in many laboratories. Various flocculation tests had by 1928 reached such degrees of sensitivity and specificity that, following comparison with the various accepted complement fixation tests at the Second Laboratory Conference of the League of Nations (Copenhagen), the better flocculation tests were considered equal to the better Wassermann tests. Similar results were obtained at the Montevideo Conference (1930) where the best of the flocculation tests were demonstrated to be superior in sensitiveness and equal in specificity to the Bordet Wassermann reaction and its modifications. The results of the American Serological Conferences (1934), in which serodiagnostic tests for syphilis used in the United States were evaluated, indicated that efficient complement fixation tests and efficient flocculation tests for blood or spinal fluid specimens are of about equal clinical value.

Additional conferences held in the United States have shown that at least 5 complement fixation and flocculation tests give satisfactory results when performed by persons other than the originators. Of the 5 tests (Eagle, Hinton, Kahn, Kline, and Kolmer) 3 are described in detail hereinafter.

APPARATUS which is needed for all the tests includes (1) test tube racks, (2) serum tubes 100 mm. long with approximately uniform 10 mm. inside diameter, (3) water bath for heating serums at 56° C., (4) Wassermann bath or bacteriologic incubator (the former is preferred) at 37° C., (5) centrifuge capable of 2,000 revolutions per minute, (6) maximum and minimum thermometer, (7) graduated cylinders of 100 c.c. and 250 c.c. capacities for measuring the reagents. Special material needed for each test will be described in detail with that test.

THE PATIENT'S BLOOD for all tests is obtained by venipuncture, allowed to clot, and centrifuged. The clear serum, free of red blood cells, is transferred to another test tube, which is then placed in a rack and heated in a water bath at 56° C. for 30 minutes. It is then ready for testing. In some flocculation tests very little serum is necessary. Sufficient blood can be collected from a finger puncture in a small capillary pipette 100 to 300 mm. in length and three mm. in inside diameter. One end of the pipette is sealed by heat, and the pipette is then centrifuged, packing cells and clot

into the lower half and leaving clear serum in the upper half. The entire pipette is then placed in the water bath at [illegible] C. for 15 minutes, making sure that the water covers well beyond the serum level. Clear heated serum is then transferred to a graduated pipette, ready for testing.

REAGENTS needed in all tests include physiologic salt solution and antigen. *Physiologic salt solution* is made by dissolving [illegible] gm. of chemically pure sodium chloride in 1,000 c.c. of distilled water. Antigens differ in different tests. Unless many tests are being done regularly it is best to purchase prepared and titered antigen. Antigen emulsions or dilutions are prepared from these stock antigens just before use. Cardiolipin antigens [illegible] especially satisfactory ([illegible] and [illegible] [illegible] 19[illegible] [illegible] 1948). Pipettes needed for preparing antigen emulsions and for delivering the serum and saline [illegible] ordinary finely graduated pipettes of [illegible] to 10 c.c. capacity.

### Kolmer Complement Fixation Test

SPECIAL REAGENTS required for the test are fresh sheep corpuscles, Kolmer antigen and amboceptor. The sheep corpuscles are washed [illegible] least 3 times, and a 2 per cent suspension is prepared by suspending 2 c.c. of washed, packed corpuscles in 98 c.c. of saline solution.

*Kolmer antigen* is a cholesterinized and lecithinized alcoholic extract of beef heart which can be bought already titered and ready for use.

*Hemolysin*.—The titered antisheep hemolysin or amboceptor can be purchased, but it is advisable to repeat the titration each time the complement fixation test is conducted.

*Stock dilution of 1:100 hemolysin* is prepared by mixing (1) glycerinated hemolysin (50 per cent) [illegible] c.c., (2) saline solution, [illegible] and (3) [illegible] per cent phenol in saline solution, [illegible] c.c. For titration, add 0.5 c.c. of 1:100 dilution to 4.5 c.c. saline. From this 1:1,000 dilution, prepare in a series of 10 tubes higher dilutions [illegible] 1:10,000. Place 0.5 c.c. of each in a series of 10 small test tubes. Prepare a 1:[illegible] dilution of complement and add 0.3 c.c. to each tube. Add 0.5 c.c. of the 2 per cent suspension of sheep corpuscles and 1.[illegible] c.c. of saline to each tube. Mix well and place in water bath at 37° C. for 1 hour. The highest dilution of hemolysin giving complete hemolysis is the unit; 2 units are employed for the actual test.

*Complement* is obtained from the guinea pig. The pig is bled from the heart into a sterile Petri dish, the blood is allowed to clot, and serum is drawn off and centrifuged to remove all cells. Complement should be kept on ice at all times.

*Dilution of Complement*.—For complement titration use 1:30 dilution.

*Dilution of Antigen*.—This is done so that the dose employed in the [illegible] is contained in 0.5 c.c. Dilution is made by placing the required amount of saline solution in a flask and adding antigen drop by drop. Shake the flask after each addition of antigen. Prepare enough antigen dilution for the complement titration and the complement-fixation tests.

*Complement Titration*.—In [illegible] series of 10 test tubes set up the complement [illegible] as follows:

| TUBE | COMPLEMENT (1:30) C.C. | ANTIGEN DOSE C.C. | SALINE SOLUTION C.C. | | HEMOLYSIN C.C. (2 UNITS) | CORPUSCLES C.C. (2 PER CENT) |
|---|---|---|---|---|---|---|
| 1 | 0.1 | 0.5 | 1.4 | 1 hr. at 37° C. for one hour | 0.5 | 0.5 |
| 2 | 0.15 | 0.5 | [illegible] | | 0.5 | 0.5 |
| 3 | 0.2 | 0.5 | 1.3 | | 0.5 | 0.5 |
| 4 | 0.25 | 0.5 | 1.3 | | 0.5 | 0.5 |
| 5 | 0.3 | 0.5 | 1.2 | | 0.5 | 0.5 |
| 6 | 0.35 | 0.5 | 1.2 | | 0.5 | 0.5 |
| 7 | 0.4 | 0.5 | 1.1 | | 0.5 | 0.5 |
| 8 | 0.45 | 0.5 | 1.1 | | 0.5 | 0.5 |
| 9 | 0.5 | 0.5 | 1.0 | | 0.5 | 0.5 |
| 10 | none | none | 2.5 | [illegible] | none | 0.5 |

The smallest [illegible] amount of complement just giving complete hemolysis [illegible] the next higher tube is the *full unit* which contains 0.05 c.c. [illegible] conducting the antigen titration and complement-fixation tests [illegible] [illegible] and are so diluted that they are contained in 1 [illegible] c.

*Kinds of Complement Fixation Methods*.—Tw[illegible] methods [illegible] quantitative test which employs [illegible] doses of serum, and (2) the [illegible] 2 doses of serum of 0.2 [illegible] and 0.1 [illegible], with an additional control. The second test is sufficient for diagnostic purposes [illegible] economical in expenditure of materials and time. The tests are [illegible] specificity.

PERFORMANCE OF THE QUALITATIVE KOLMER TEST.—For [illegible] arrange [illegible] test tubes (1), (2) and (3). Place in them the saline solution: Tube 1, 0.[illegible] [illegible] Tube 2, 0.5 [illegible] and Tube 3, [illegible] 0.[illegible] [illegible] of inactivated serum. Mix by drawing up in the pipette [illegible] 0.[illegible] [illegible] to Tube [illegible] [illegible] Tube [illegible] the serum of Tube 2 and discard 0.[illegible] c. from it. This leaves 0.5 [illegible] in each which carry 0.2 and 0.1 [illegible] of serum respectively. New Tube [illegible], of which 0.2 [illegible] is serum. Place 0.5 [illegible] of the proper [illegible] Tubes 1 and 2 and also into [illegible] control tube carrying 0.2 c.c. [illegible] Since Tube 3 receives no antigen the total [illegible] in all tubes [illegible] is [illegible]. Allow tubes to stand for 10 to 20 minutes. [illegible] complement (1.0 [illegible] c.) to each tube [illegible] control tube [illegible] hemolytic system control. Then set up [illegible] control by [illegible] 0.5 c.c. of the 2 per cent suspension. [illegible] tubes gently [illegible] [illegible] to [illegible]° C. for 15 to 18 hours. Th[illegible] place tubes in water [illegible].

minutes, not longer. To each tube, except the corpuscle control, add 2 units of hemolysin and then 0.5 c.c. of 2 per cent corpuscle suspension, which has previously been well shaken. Mix the contents of the tubes by agitation, place in water bath at 37° C. 1 hour and then read the tests. The tubes may be placed in a refrigerator for an hour or two before making the readings. More sensitive readings may be made 10 minutes after the antigen control, the hemolytic system control and the serum control show complete hemolysis. Reading at this time is preferred. Serum control, hemolytic system control, and antigen controls should be completely hemolyzed; the corpuscle control should show no hemolysis.

RESULTS.—

*Strongly Positive.*—Complete fixation, 4-plus, in first and second tubes.
*Moderately Positive.*—Complete fixation, 4-plus, in first tube only.
*Weakly Positive.*—Partial fixation in one or both tubes.
*Doubtfully Positive.*—Plus-minus in first tube.
*Negative.*—Complete hemolysis in both tubes.

### Kahn Precipitation Test

SPECIAL APPARATUS needed includes a *shaking apparatus* to insure the adequate mixture of the reagents used in this test. There are several types of shaking apparatus available.

ANTIGEN for the Kahn test is cholesterolized (0.6 per cent) ether-insoluble alcoholic extract of beef heart. This may be purchased already prepared and titered. *Antigen suspension* or *dilution* is prepared by mixing the antigen with physiologic salt solution according to the required titer. Thus, if the titer is 1 c.c. antigen plus 1.1 c.c. salt solution, proceed as follows: Measure 1.1 c.c. salt solution into a standard antigen suspension vial and measure 1 c.c. antigen into a similar vial. Pour the salt solution into the antigen, and, as rapidly as possible without waiting to drain the vial, pour the mixture back and forth 6 times to insure thorough mixing. Allow the antigen suspension to stand 10 minutes before using. The suspension should not be used after 30 minutes' standing.

PERFORMANCE OF THE STANDARD TEST. Set up the test tubes in a rack, using 3 tubes for each serum to be tested. Shake the antigen suspension again before using, and deliver 0.05, 0.025, and 0.0125 c.c. amounts to the bottoms of the tubes of each 3-tube set. Add 0.15 c.c. of clear heated serum to each tube, and shake the rack of tubes vigorously for about 10 seconds. Each serum should be examined for particles which might give the appearance of specific precipitate. If particles are present, the serum should be cleared by centrifuging it again. Place the serum-antigen mixtures in a water bath at 37° C. for 10 minutes, then shake by machine or hand for 3 minutes. Add 1 c.c. salt solution to each tube of the first row of the rack, the row of tubes each containing the 0.05 c.c. amounts of antigen suspension, and add 0.5 c.c. of salt solution to the remaining tubes. Shake sufficiently to mix ingredients, then read results.

CONTROLS.—(1) Antigen. When pipetting antigen suspension for a series of tests, use as control the farthest right set-up of 0.05, 0.025 and 0.0125 c.c. amounts, adding to each tube 0.15 c.c. of salt solution instead of serum. All 3 tubes should show freedom from precipitation. (2) Serum. Include with each series of tests one or more serums which are known to give positive reactions and a similar number giving negative reactions.

#### TABULAR OUTLINE OF THE TEST

| | *Tube 1* | *Tube 2* | *Tube 3* |
|---|---|---|---|
| Serum-antigen suspension, ratio | 3:1 | 6:1 | 12:1 |
| Antigen suspension, c.c. | 0.05 | 0.025 | 0.0125 |
| Serum heated at 56° C. for 30 minutes, c.c. | 0.15 | 0.15 | 0.15 |

RESULTS.—Reactions are read on a plus-sign basis, ranging from 4-plus to 1-plus, depending on the size and visibility of the particles suspended in the medium.

*Positive Result.*—Definitely visible particles are suspended in a transparent or opalescent medium. The individual particles are readily visible by direct examination.

*Doubtful Result.*—If the particles are extremely fine and just within the visible range, the reaction is called doubtful.

*Negative Result.*—If the medium is transparent and opalescent and free from visible particles, the reaction is called negative.

### Performance of Quantitative Tests

DILUTION.—While different methods of dilution have their advocates, the simplest is a twofold serial procedure, prepared by placing 1.0 c.c. of diluent in each of 6 to 10 tubes. To the first is added 1.0 c.c. of inactivated serum. This is thoroughly mixed by drawing it up in the pipette several times, then 1.0 c.c. of the mixture is transferred to the second tube. This process is repeated with all the tubes in the series, so that the final dilutions are 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512, and 1:1024. If only 0.3 c.c. of serum is available for quantitative testing, then 0.3 c.c. of diluent is placed in each tube, and to the first is added exactly 0.3 c.c. of inactivated serum. After thorough mixing, 0.3 c.c. of the mixture is transferred to the second tube, and again the process is repeated with all the tubes in the series. The final dilutions are again 1:2, 1:4, 1:8, etc. It is important that the mixing be thorough and uniform in each tube. Care must also be taken to remove any excess of serum on the outside of the pipette before making the transfer to the next tube.

DILUENT.—Variations in final titers may occur if different diluents are employed. Some serologists advocate the use of pooled negative serum as a diluent, but the titers obtained are usually much lower than if physiologic saline is used. Different lots of negative serum may give noticeable variations in the titer. Various preparations of physiologic saline may differ in their electrolyte content and the resulting hydrogen-

ion concentration of the solutions. These variations may also affect the final quantitative results. It is suggested, therefore, that a buffered saline solution with the following formula be used as the routine diluent for quantitative testing: $Na_2HPO_4$ (anhydrous) 11.3 gm., $KH_2PO_4$ 2.7 gm.; NaCl 170 gm.; distilled water to 1000 ml. Add 50 ml. of this stock solution to 1000 ml. of distilled water for use as a diluent.

METHOD OF REPORTING.—The method advocated by Harris (VDI 28: 249, 1947) is simple and adequate: the quantitative serologic reactions are reported in terms of the greatest dilution in which the specimen tested produces a positive reaction, and that the term "dils" (a contraction of the word "dilutions") is used to identify the end point of dilution reactivity. For example, a report of "32 dils" indicates that the tested serum gives positive reactions in dilutions up to and including, but not greater than, 1 to 32. Confusion would diminish if uniform methods of diluting serums were employed, if similar and reproducible diluents were utilized, and if a simple method of reporting the quantitative results were adopted.

**Evaluation of Serologic Tests.**—Interpretation of laboratory reports requires considerable knowledge of serology. Reliability of a laboratory depends to some extent on the volume of work done, meticulous adherence to standardized methods, and frequently repeated checking with other good laboratories. It is fundamentally a mystery why a lipid extract of tissues of a normal animal reacts with the serum of a syphilitic human being, and it is true that the sera of some nonsyphilitic persons, as well as the sera of persons suffering with diseases other than syphilis, give syphilitic reactions on testing. The biologic false positive cannot be distinguished from the truly positive (Rein and Elsberg: JInvD 6: 113, 1945), although complex procedures under investigation by Kurath et al. (AmJS 31: 347 ff, 1947) make it hopeful that the puzzle may be answered.

Quantitative testing is becoming routine, early encouraged by Moore and Eagle (AnnIntM 14: 1802, 1941). When a low titer persists after adequate treatment, no further treatment is indicated unless the titer rises significantly, according to Thomas (AmJS 30: 81, 1946). Clinical relapse is regularly heralded by rise of titer. Persisting high titer after presumably adequate treatment justifies continuation of therapy. In neurosyphilis, the spinal fluid findings, not those of the blood, are the reliable guides. Variation in titer is puzzling, especially in low titer patients, where a test may be negative at one time and weakly positive at another; this is sometimes due to variation in the sensitivity of the test (Mohr and Smith: AmJS 24: 322, 1940). Extremely sensitive tests give more false positives but miss few actual cases, and less sensitive testing technic yields positives more to be trusted but misses some weakly positive cases (Tuft and Richter: AmJS 23: 731, 1939). Test technic was described in detail for several standard tests in VDI Suppl. 9, 1939. Hinckelsen (Suppl. 14, 1941) reviewed the subject in detail. The anticomplementary test sometimes means the titer is extremely high (Carter: ADS 46: 843, 1942). Discrepancies between results of testing the same serums with different tests were studied in detail by Mahoney (NYSJM 43: 843, 1943).

**False Positive Tests** may be due to technical error avoided by requesting several different procedures to be done on the same serum by different laboratories. One never diagnoses syphilis on the basis of the report of one test. When the test is positive because of the existence of nonsyphilitic disease, the positivity is as a rule transient, lasting for only a few weeks or months, and as a rule the titer is not high.

Disorders which induce pseudosyphilitic positivity include upper respiratory infections, vaccination against smallpox, infectious mononucleosis, typhus, filariasis, hyperproteinemia, varicella, injections of foreign protein such as tetanus toxoid, infectious hepatitis, malaria, leprosy, tuberculosis, lymphopathia venereum, leishmaniasis, and scarlet fever. Syphilitic reaction occurs in yaws, pinta, rat bite spirochetosis, relapsing fever and other spirochetal infections. Before interpreting tests as indicative of syphilis, consideration must be given these possibilities (Mohr et al.: AnnIntM 7: 322, 1946; Beerman: AmJMSc 209: 525; 210: 654, 1945; Albrecht: CurMDig, July 1947; Stokes et al.: J 130: 57, 1946).

Many normal animals give positive tests (Kemp et al.: AmJS 24: 637, 1940). The biologic false positive persisting in a normal human being cannot be distinguished by serologic methods (Scott et al.: AmJS 29: 603, 1943). Persistent positivity justifies the administration of adequate treatment now that Mapharsen and penicillin make such a recommendation less hazardous to the patient than this advice would have been a few years ago.

**Prognosis.**—The earlier one institutes treatment and the more thoroughly it is carried out, the better the outlook, in general. Unfortunately the consequences are sometimes disastrous in spite of or because of the treatment.

Alcoholism, tobacco and mental, physical, and sexual excesses are detrimental to the welfare of the patient. The location of the initial lesion exercises no influence upon the aftercourse of the disease. In patients whose syphilis is thoroughly treated, the probability of late complications is diminished. Nevertheless, the disease may materially lessen life expectancy in men with acquired syphilis this is shortened from that of the general population in the age group 30 to 60 years by 17 per cent in the white and by 30 per cent in the Negro Usilton and Miner (VDI 18 231, 1937) reported from their study of Cooperative Clinical Group material.

Review of actuarial studies by Schamberg (AmJS 29: 539 1945) showed that the best figures indicate that the well-treated group had an appreciably higher mortality a fact probably due to factors of selection. Schamberg concluded, There is no evidence that syphilis adversely influences life expectancy except through the known lethal effects of its serious late manifestations, in particular those of the central nervous and cardiovascular systems. There is no evidence that syphilitic infection per se or antisyphilitic treatment predisposes to tuberculosis, pneumonia, nephritis, or other nonsyphilitic diseases. Increased mortality in syphilitics is caused in part by deaths due directly to syphilis, in part to the higher death rate in segments of the population which have a high syphilis prevalence. Adequate antisyphilitic treatment will in the majority of cases *prevent the late manifestations of syphilis*. Employers may safely hire syphilitics. The incidence of cardiovascular syphilis is inversely proportional to the amount of treatment received in the early stages of the disease, ranging from 18 per cent in untreated cases to 0 4 per cent in those adequately treated (Kemp and Cochems AmJS 21: 625 1937) Moore and Schamberg (J 134: 1532 1947) stated that the applicant with untreated syphilis in any stage should be granted life insurance if the applicant can demonstrate good health; in all patients the spinal fluid should have been shown by adequate and reliable tests to be normal after adequate treatment and not earlier than 8 years after infection. See JVDI 27: 34-52, 1946

The outlook intimately depends on treatment. Stokes et al. (AmJMSc 188 669 1934) in the Cooperative Group studies, stated that relapses diminish as the number of arsphenamine injections increase. Continuous treatment is to be preferred to intermittent irregular or intensive attack. Arsphenamine does not predispose to central nervous system involvement, but irregular treatment certainly does. For best results, seronegative primary cases should have 10 to 20 arsenical injections seropositive primary, 25 to 35 and the early secondary cases, 20 to 30 A heavy metal should be given in courses in all types. Adequate treatment for 2 years yielded symptomatic cure of 96 per cent of early cases, while inadequate treatment cured only 73 per cent. Any treatment is better than none, yet neurosyphilis was 3 times as common in the poorly treated cases as in the untreated series.

Comparable statistics regarding the outcome in patients treated with penicillin cannot be compiled for a number of years, for the drug was first used in 1943 but its striking effectiveness in early syphilis and in meningovascular neurosyphilis has been most encouraging (Moore et al. J 126 67 1944 Stokes et al. ib p 73)

About one-fourth of all patients who contract syphilis can expect spontaneous cure without treatment and another fourth achieve complete latency About one-sixth of all syphilitics who develop positive serologic tests will remain seropositive with or without treatment.

UNTREATED SYPHILIS.—Bruusgaard (AfDuS 157 309 1929) surveyed the 2,181 patients who were given no specific treatment by Boeck, who from 1891 to 1910 at Oslo preferred no treatment at all in early syphilis to the mercurial treatment then in vogue This carefully studied un-

treated series served as the control in the Cooperative Group review of the effects of treatment in early syphilis. Comparison of treated with untreated syphilis (Sowder AmJS 24 684, 1940) showed that (1) central nervous system relapse is 2 to 4 times as frequent in untreated cases (2) cutaneous and osseous relapses are 17 to 26 times as frequent in untreated cases (3) treatment results in freedom from symptoms in 77 per cent if adequate and 63 per cent if less than adequate, while no treatment is followed by freedom from symptoms in 24 to 36 per cent (4) in cases of seronegative primary infection, despite treatment there occurs 1.2 to 1.5 per cent incidence of spinal fluid abnormality within 3 to 20 years (5) adequate treatment results in freedom from symptoms in 96 per cent, while no treatment is followed by freedom from symptoms in 61 per cent of cases in the 3- to 10-year period, while in the 10- to 20-year period, treatment has the advantage of 74 as compared with 50 per cent freedom from symptoms (6) syphilis is relatively benign, but it is worth treating (7) irregularity of treatment seemed the chief cause of complications. Low dosage of arsenicals with intermittence of treatment resulted in a high incidence of neurosyphilis. Continuous treatment for 2 years cured 86 per cent of seronegative primary cases, 64 per cent of seropositive primary cases, and 81.5 per cent of secondary cases. A florid secondary eruption seemed an advantage.

Autopsies of 380 untreated syphilitics revealed anatomic lesions of syphilis in 39 per cent and no such lesions in 61 per cent, while 23 per cent of the series died as a result of syphilis, a death rate approximating that of Bruusgaard's series, as reported by Rosahn (JVDI 27 293 1946). Some 17 per cent of these persons had achieved spontaneous cure without treatment.

TREATED AND UNTREATED SYPHILIS. COOPERATIVE CLINICAL INVESTIGATION AND BRUUSGAARD'S SERIES

| | Grouping by years after infection | Incidence in groups: Treated | Incidence in groups: Untreated |
|---|---|---|---|
| | (years) | (per cent) | (per cent) |
| 1. Relapse in the form of clinical involvement of central nervous system | (3 10)<br>(10 20) | 1.4<br>0.2 | 6.1<br>16 |
| 2. Relapse in the form of cutaneous, mucosal, and osseous lesions | (3 10)<br>(10 20) | 2.0<br>1.2 | 34.5<br>31 7 |
| 3. Symptom free cases with positive Wassermann | (3-10)<br>(10 20) | 17.0<br>16 3 | 36.7<br>15.6 |
| (The similarity of proportions in treated and untreated cases of the 10 20 yr group suggests that about 13 per cent of fixedly positive Wassermann cases is perhaps an irreducible minimum.) | | | |
| 4. Symptom free cases with negative Wassermann | (3-10)<br>(10 20) | 77 0<br>62 8 | 24.0<br>36.4 |
| 5. Cardiovascular symptom | (3 10)<br>(10 20)<br>(20-30)<br>30 40) | 0.7 1.3(?)<br>5.8 10.4(?)<br>?<br>? | 0 (unrecognized ?)<br>1.5<br>10 0<br>12.5 |
| 6. Symptom-free cases serum positive or negative | <br><br>(3 10)<br>(10 20) | (Adequate treatment)<br><br>96 0<br>74.0 | (No treatment)<br><br>60.7<br>30.0 |

Toxic reactions to arsenicals probably do not affect the status of the disease favorably or unfavorably excepting so far as they may signify that it is impossible to use arsphenamine in the case

**Prophylaxis.**—A oblance of exposure to *S pallida* can be depended on to prevent infection. The admonition to avoid exposure is wholly futile for the human herd is promiscuous. It is generally possible to prevent infection despite a syphilitic contact if advantage is taken of the antiseptic effects of the prompt and generous use of soap and water followed by th diligent application of Metchnikoff's paste, which is 33 to 50 per cent calomel in hydrous wool fat and petrolatum. The Army prophylactic kit a single tube containing 30 per cent calomel and 15 per cent micronized sulfathiazole achieved a failure rate of 0.13 per cent (BullUSAMD 6 _3 1944) Mechanical separat on of presumptively infected tissues from those to be kept pure is probably best (Cautley et al. AmJMSc 193 153 1938) Moist sores teeming with spirochetes are not regionally limited to genital distribution. See Stokes (VDI 23: 183, 194 ) and Eagle et al. ( AmJS 31 _37 194 )

The maintenance of an adequate level of bi muth by injecting a suspension of it into prostitutes every week may keep them noninfectious (Hamlik et al. AmJS 4 469 1940)

If the possibility of infecti n has been incurred, and the time for prophylaxis has passed, one does not know whether inoculation ha actually taken place. We believe t wise then to wait and p ove the existence of infection before giving specific therapy To know pos tively whethe patient i infected is a matter of vital importance to him, and worth waiting for

**Control.**—A a publ h health problem, syphilis ha been attacked with vigor in the United States Heller ( AmJS 31 569 194 ) gave the death rate as 16 per 100,000 in 1936 and estimated it a 0 3 per 100,000 in 1946, wh le infant deaths from syphilis dropped from 69 to _3 He quoted a basic the 9 princ ples f control advocated by Parran provision f an a lequate and adequately trained public health service staff case finding and case holding premarital and prenatal serodiagnosis, provision of free diagnostic services provi on of treatment facilities, distribution of drugs for therapy routinization of serodiagnostic test the dissemination of scientific information, and public education. The effort f the New York City Health Department were simila and ffect e a described by Rice ( AnnIntM L 503, 1938) Case finding and case holding the tracing f co tacts, and inducing patients once gotten under treatment to persist in treatment were discussed by Wood (VDI 20 3 1 1939) Practical problems were reviewed by Stokes (AmJS 23 549 1939) Contact tracing i a valuable and successful effort (Casselman and Cadwallader VDI 20 183, 1939) While professional prost tution is relat vely unimportant statistically it must energetically be ppressed it generally agreed (Clark VDI 1: 349 1940 Stokes VDI _3 193 194 Williams CanadPHJ 31 461 1940) Amateurs of the civilian public were the greatest hazard t the Armed Forces. Contact tracing sustained by quarant ne a thor ty an disclose numerous infectious individual and bring them under treatment (Freeman OhioSMJ 36 616 1940) R pid treatment centers established during the war emergenc and most creditabl managed in the United States by Wile contributed greatly to the control ffort A especially remunerative method of case fin ling the serologic testing f large groups f d i luals ( Anderson et al : J 130 993 194 and this measure deserves t be promulgated. Cooperative and diligent enterprise of all concerned with the public health s requisite.

**Treatment.** —See also articles on particular drugs in the chapter on treatment and in the section on dermatitis medicamentosa. Syphilis usually responds readily to appropriate treatment although some of its results are disastrous in spite of approved methods of attack. The disease has often indeed been mistreated. Sound but dated reviews of treatment, emphasizing the need f r prolonged and continuous therapy are those of Stokes and Usilton ( ADS 35 377 1937) Moore et al. (J 116 2405 1941) Padget ( AmJS 24 692, 1940) and Cole (J 117 1091 1941) No one today claims to kn w the best possible way to treat syphilis, but excellent and effective treatment can be planned

**General Measures.**—One important step is education of the patient. His health should be carefully observed and maintained at the peak Ober

mayer and Becker (ADS 34 57 1936) recommended ultraviolet light baths, rest and autohemotherapy Secondary anemia is usual in syphilis, and suitable tonics are worth giving The teeth should be kept well and the gums healthy because metals are then better tolerated Sore gums in clinic patients are often due to scurvy Focal infection should be sought out and remedied especially in resistant cases.

**External Treatment.**—Cleanliness and hygienic measures are important. In initial lesions calomel is a good dusting powder In mixed lesions due to infection with both *S pallida* and *H ducreyi* local treatment is as for chancroid. Cauterization or excision of a chancre is futile Nonulcerative syphilids require no local treatment The regression of pustular lesions may be hastened by moist applications of 1 5 000 bichloride of mercury Ulcerative lesions may be covered with moist bichloride packs or 2 per cent ammoniated mercury ointment Ulcers in a syphilitic patient may be due to streptococci carcinoma, or other diseases, just as in nonsyphilitic individuals.

**Principles of Treatment.**—Best treatment of early syphilis in the prepenicillin era entailed (1) early correct diagnosis (2) the use of drugs of proved worth; (3) continuous treatment without rest periods (4) a treatment period of an arbitrary minimum of 12 to 18 months, (5) determination of cure only by lifelong posttreatment observation and (6) the avoidance of poisoning the patient (Moore AnnIntM 10 30, 1936) Continuous therapy the injections being given at regular intervals without rest periods, The American System, is believed to be best. The duration of the period during which chemotherapy is actually administered is considerably diminished with the use of penicillin. Treatment must be purposeful individualized, and carefully planned and executed. The patient must be brought to trust his physician and to cooperate intelligently and willingly

Treat the patient, not his blood (Moore) When a patient has latent syphilis and has received adequate treatment he should be let alone except for periodic titered serologic tests and checkup physical examinations. One must remain continuously aware of the hazards of any therapeutic agents used seeing to it that the treatment is not worse than the disease. The large proportion of syphilitic infections are comparatively benign and harmless. Mental and physical breakdowns have been precipitated by persistence in misguided therapeutic measures, overtreatment being responsible for depression emotional instability fatigue weakness, loss of weight and nervous irritability (Cornia CanadMAJ 40 446 1939)

Clinical cure is usually achievable and the patient should be given encouragement and reassurance While almost all physicians treat syphilis, few are syphilologists. A wise physician is humble, admits his doubts to himself and takes advantage of consultation with experts.

**Favorable Response to Therapy** measured by disappearance of spirochetes from sores healing of visible lesions, diminution of titer of quantitative serologic test improvement in the spinal fluid formula, manifestation of well being of the patient such as gain in weight and in ability to perform mental and physical work which syphilis handicapped prior to treatment and relief of symptoms of the myriad varieties for which syphilis may be responsible Quantitative serologic studies by Beall et al (AmJS 4 29 1940) showed that chemotherapy reduced the titer in about a third of the cases of late acquired syphilis and half the cases of congenital syphilis; arsenicals reduced the titer twice as much in early syphilis as in late.

One should not be stubborn in attacking the blood test, for at least 15 per cent of all syphilitic positives remain so no matter what is done. The absence of necessity for reversing serologic tests must be explained to the patient if he falls into this unfortunate group who are frequently subjected to overtreatment, its hazards and its costs, and who frequently develop syphilophobia. See latent syphilis.

**Relapse.**—Within 2 years after cessation of treatment, most relapses which are to take place have done so. Relapses under continuous treatment occurred in 11 per cent, under intermittent treatment in 21 per cent, under irregular treatment in 43 per cent, and after intensive treatment in 41 per cent (Cole: J 107: 123, 1936). Arsphenamines and penicillin are especially spirochetícidal and are necessary to prevent infectious relapse.

**Neurosyphilis and Early Treatment.**—Asymptomatic neurosyphilis was found in 13.5 per cent of 5,300 patients of O'Leary et al. (ADS 35: 25, 1937). Adequate treatment of early syphilis was followed by an incidence of spinal fluid abnormality of 7.5 per cent, and irregular treatment by 22.6 per cent. Of those with abnormal spinal fluid 14 per cent had negative blood tests. The less the degree of spinal fluid abnormality the better the response to therapy proved to be. If treated syphilis remained latent, the spinal fluid remained so in 99 per cent of the cases. Serologic relapse warrants another examination of the spinal fluid. Seroresistance of 4 years duration or more was associated with 75 per cent incidence of central nervous system involvement. It appears that penicillin therapy of early syphilis (q.v.) is followed by a notably low incidence of neurosyphilitic relapse.

**Pregnancy.**—Treatment of 116 women during pregnancy with mapharsen and bismuth was followed by 94.7 per cent live births in the 76 patients who received 8 or more treatments (Castello et al.: AmJS 23: 332, 1939). *Danger of severe reactions among pregnant women treated intensively with arsenicals is greater than is generally realized* (Ingraham: J 112: 1537, 1939). The pregnant woman is not exempt from any of the more severe types of reaction of intolerance, including fatal hemorrhagic encephalitis, acute circulatory collapse, hepatic damage, dermatitis, and aplastic anemia. Treatment of syphilis during pregnancy does not increase the liability to toxemias of pregnancy (Peckham: AmJS 25: 280, 1941). It is essential that all seropositive pregnant women receive treatment in order to prevent prenatal syphilis. The effectiveness of penicillin and its safety in pregnancy render out-of-date studies of the use of less recent agents. Penicillin can be used successfully late in pregnancy if the child is still viable (Cole et al.: ADS 54: 255, 1946). It should be used routinely (Goodwin and Moore: J 130: 633, 1946).

**Surgery in the Presence of Syphilis.**—In undertaking surgery upon syphilitic individuals, there is a real but small risk of acquiring syphilis by accidental inoculation. As to the patient, there is an ideal focus for the development of acute syphiloma in a surgical wound. In preparation for operation 2 or 3 doses of arsphenamine along with doses of bismuth during a period of 2 weeks suffice to protect against untoward results (Wile: CalWM 49: 7, 1938). Penicillin should be used.

**Tuberculosis** does not contraindicate the treatment of concomitant syphilis, unless the medicament schedule is too intensive (QMN: J 1: 4, 398, 1944). Penicillin is well tolerated and efficient.

**Diabetes** accompanied by syphilis was studied by Perkin (AnnIntM 21: 275, 1944). When 19 such patients were treated for syphilis, their diabetes improved. There seemed to exist a relation between syphilis and gangrene occurring in mild diabetics. It is doubtful that syphilitic diabetes occurs, however (McDaniel et al.: AIntM 66: 1011, 1940).

**Marriage** should be undertaken by a syphilitic person only after he has undergone a complete course of adequate treatment and after he has remained free from evidence of the disease for a considerable period after the termination of active therapy. Certainly 2 years and preferably more should have elapsed from the time of infection. When the infection was 5 years old at the time of marriage 30 per cent of the partners became infected but after the tenth year the likelihood of the normal partner's acquiring the disease was almost nonexistent (O'Leary: PSMMC 15: 1, 1940).

***Chemotherapy.**—In the specific treatment of syphilis, 5 drugs are known to be effective: penicillin, arsenic, bismuth, mercury and iodine. Adequate treatment is usually harmless in tuberculous patients. Adequate treatment, desirable, is usually tolerated in pregnancy. Sulfonamides and streptomycin are among the drugs which are not useful in syphilotherapy.

**The Ideal Antisyphilitic Drug** should possess a high chemotherapeutic ratio, that is, it should be of low toxicity to the human being and of high potency against the spirochete. It should be easily administered and inexpensive. Penicillin possesses all these qualities. The arsphenamines and Mapharsen are the ideal agents for eradicating acute infectious lesions of syphilis. In using bismuth preparations it is necessary to administer the salt frequently enough to keep continuously a therapeutic level of the metal in the blood stream [this is true also of mercury]. This may be conveniently measured in the form of the terms of excretion of bismuth in the urine, around 3 to 4 mg of bismuth daily (Cole VDI 19: 6, 1938). When a rapid bismuth action is desired the water soluble preparations are indicated; for slower and more sustained action, the oil soluble or oil suspended preparations are t be selected.

**Toxicity**.—To treat syphilis wisely toxicology of the drugs used must constantly be kept in mind. Each may be poisonous. See dermatitis medicamentosa.

In investigations of toxicity use is made of the terms *maximum tolerated dose* (M.T.D.) *minimum effective dose minimum curative dose therapeutic index* (M.T.D. divided by M.E.D.) and *curative index* (M.T.D divided by M.C.D.). Grohalt (ADS 32: 848, 1935) stated that T.I. of Mapharsen is 18, of arsphenamine is 14, of neoarsphenamine is 9; C.I. respectively is 9 11.6 and 8.3. Cole (1936) gave the therapeutic index for arsphenamine as 20 1 to 30 1 bismuth intramuscularly 60 1 and mercury 1 1 to 1 2.

**Arsenicals.**—Ehrlich s salvarsan, or arsphenamine, the 606th preparation of a series of synthesized compounds, is dioxy-diammo-arsenobenzene dihydrochloride. It is a yellow powder containing 31 per cent of arsenic, soluble in water forming a strongly acidic solution. The average practical dose of arsphenamine for an adult was 0 40 gm (6 grains) and the drug was given, *after neutralization* intravenously. When ingested, it is poisonous. Exposure to the atmosphere results in oxidation, deterioration, and the formation of toxic substances.

Various arsenicals are given intramuscularly subcutaneously or intravenously. Acetarsone is given by mouth. Neoarsphenamine may be given to infants intramuscularly and sulfarsphenamine was so given to adults. The subcutaneous route is likely to cause slough. The usual route is intravenous.

Mapharsen (Mapharsen) the arsenoxide responsible for the activity of the arsphenamines, has superseded old arsphenamine and most f the later variations t was used in many thousands of doses as the standard therapeutic agent in the military services of the U.S.A. in World War II with notably few serious reactions. Its chemistry and effectiveness have been reported by Hem and W se (J 113 1946 1939) Chargin et al. (ADS 40 208, 1939) Stokes and Beerman (AmJMSc 201 601 1941) Long (ADS 47 226, 1943) Guy (ib. p. 235) and many others.

Clorarsen (3 amino-4-hydroxyphenyl dichlorarsine hydrochloride) was introduced by Tompsett et al. (JPhExpT 73 412, 1941) reporting results favorable as compared with other arsenicals. Kampmeier and Henning (AmJS 47 208, 1943) Beerman and Wammock (ib. 31 150 1947) and others have found it relatively safe and satisfactory. The maximum dose is 0.075 gm.

Many other arsenicals have been synthesized and studied (Eagle et al. JPhExpT 69 343; 70: 211 221, 1940) but the practitioner adheres to conservatism in his selection of medicines for his patients.

**Technic of Administration of Arsenicals**.—Arsphenamine.—All apparatus and solutions must be sterile. Freshly distilled, dependably pure water should be employed. Gravity infusion is safer than injection by syringe. The ampule is tested by immersion in alcohol. If intact its content is sprinkled int a known quantity of water which contains a drop of phenolphthalein, and 0 85 c c. normal sodium hydroxide per 0 1 gm. arsphenamine is added. Dilution is mad up with water to 25 c.c. per 0 1 gm. of rsphenamine. The solution, filtered, must be clear and alkaline (pink). It is injected slowly nt the vein, at the rat of 0 1 gm. arsphenamine per minute with great care not to infiltrate outsid the vessel. This information is of historic interest only.

Neoarsphenamine ( 914 ) contains 20 per cent of arsenic, and is more readily soluble in water than Salvarsan. Neoarsphenamine is dissolved in 2 c.c. of water per

0.1 gm. of the drug and given intravenously at the rate of 0.1 gm. neoarsphenamine per minute. Of neoarsphenamine 0.6 gm. is equivalent to 0.4 gm. of arsphenamine.

MAPHARSEN is given in doses of from 0.04 to 0.06 gm. Aeration does not increase its toxicity nearly so much as it does that of arsphenamine and neoarsphenamine. After it is dissol ed, it i gi en rapidly in order to diminish the pain in the arm which is a common complaint. Promptl applied cold compresses relieve this pain when it occurs.

TRYPARSAMIDE has been thought valuable in neurosyphilis, given in doses of from 1 to 3 gm. intravenously at weekly interval. It may be combined judiciously with fever therapy. It has a good tonic effect, but is less effective than malaria, and entails danger of optic nerve damage. It is not spirochetickidal and is not used for that purpose (Hinrichsen ADI 20: 293 1939). It has been abandoned in modern therapy because penicillin either alone o with fever gives superior results and because Tryparsamide is a dangerous drug (Moore).

**Reactions to the Arsenicals.**—Herxheimer's reaction is a temporary inflammatory aggravation of the symptoms, which usually occurs following the first administration of spirochetic lol arsenicals. It is attributed to enhancement of allergy by the killed spirochetes. Thi sudden symptomatic flare is carefull to be avoided when the optic nerve audit ry ers or aorta is involved, for the result of too vigorous treatment may be extremely harmful. Se dermatitis medicamentosa, arsenic p. 101. See excellent study of Farmer (J 138 480 1948).

**Abortive Arsenical Treatment and Rapid Treatment Plans.**—The hope of terilizatio magna has persisted ince Ehrlich first imagined it had been attained. *Pollitzer (JCutD 4 633 1916) attempted a rapid treatment plan,* but the proportion of cures did not exceed 3 per cent. Cooperat ve Cl nical Group studies (VDI 13 0 103) indicated that the tedious standard method yielded 79 per cent satisfactory results. Chargin et al (J 104: 878 1933 AmJMed 19 450, 1939) howed that chemotherapy by massive doses of arsenicals given by intra enous drip was effective (see J 114 343 1940). Early syphilis may be so treated the outstanding dvantage being that d ring a brief hospitalization the patient completes treatment of the infection stage. The total dose using Mapharsen must exceed 1.0 gm. (Thomas and Wexler ADS 4 533 1943). Various schedules ma be employed, using the multiple syringe techni intra enous drip, or combinations of arsenicals with fever induced by typhoid vaccine or other mean (Schaffer ADS 3 147 1943) the results being approximately equivalent. Chargin et al. (ADS 4 38 ff 1940) gi e 0.4 gm. Mapharsen in ,000 cc f 5 per cent dextrose i 8 hours dail for 5 day. Rattner (J 1 : 964, 1943) a ded a dail i jection f 0.022 gm. b smuth sodium tartrat and reported 85 per ent successes. Neoarsphenamine proved unsati factory causing a high incidence f peripheral neuritis.

The incidence of severe general reactions approaches 100 times that experienced with the use f conservat method (Cole et al. J 123 33 1943) yet ad antages under suit ble condition f complete an l expert control make the procedure nevertheless acceptable. Hemorrhagic encephalitis is the complication most to be feared for it was ommonly f tal p t the development f BAL, which sa ed the l es f the 12 patient of H ller (AnnI tM 31 194 ) wh developed agran locytos while undergoi g ant syph l tic reatment.

Hepat tis neurit dermatitis fe ou t g pai n the arm, thrombosis and all other kind of poison g w th arsenic may occu. Massive treatment prior to BAL killed about 3 patient pe 1,000 in the most competent hand.

The posit e pressure tourniquet test becomes positive prior to the clinical appearance f hemorrhagic complicat on, serving a a valuable warni g (Curtis J 126 333 1944).

The most effect ma si chemotherapy yield 93 t 90 per cent of satisfactory esult n pr mary syph l and 0 per cent n secondary relapses being approximately 3 per cent i the former group nd 1 per cent n the latter according t evaluation studies f 4 331 treatment J 126 333 1944). Bismuth, given too, improved the statistics pparentl. Pat ent over 3 ears f ge d d better than younger ones the oung Negro f males were most often se ousl intoxicated.

**Curative Dose of Mapharsen.** rapid treatment plans i not largely affected b the frequenc nd duration f treatment nd the best schedule ut lizes the shortest period wh h curat dosag be given safely (Eagle and Hogan VDI 25 139 1944). The cur t dose the se rity f 20 t 30 mg./kg., i t 1.4 gm. for the a erage adult. Schedules briefer than 20 da re not saf. If the total dose is divided mong 3 jectio per week for 7 week intoxication is comparatively low. It resulted n terrupt n f treatment n 106 f 4,523 patient with 39 serious intoxication mostly j undice a d 4 death (Eagle J 126 339, 1944). Schock and

Alexander (AmJS 28: 221 1944) reported 20 per cent failures with this schedule The administration of 20 doses of Mapharsen and 10 of bismuth in 10 weeks resulted in seronegativity in 89 per cent of the cases of Dexter (AmJS 533 1947) and may be considered extremely effective in early syphilis; yet many patients failed to complete their treatment

**Bismuth** has almost completely supplanted mercury The salicylate in oil, sodium potassium bismuth tartrate in water and Iodobismitol are in common use The drug is less nephrotoxic than mercury and may be used particularly in the treatment of late syphilis, with less emphasis on the arsphenamines in these cases. Its concomitant administration during treatment with arsenicals or penicillin may be expected to improve the likelihood of cure It is generally given in oil suspension once a week either during the administration of more potently spirochetocidal drugs or in courses alternating with them (Kahn and Becker J 120 338 1942) In tolerance is evidenced by lassitude sore mouth arthralgia and myalgia and gastrointestinal symptoms (Walsh and Becker J 116 484 1941)

Bismuth is effective in doses such that a therapeutic level of the metal is kept in the blood, most easily measured by urinary excretion. An adequate level of bismuth urinary excretion can be maintained by the injection three weekly of aqueous or ethylene glycol solutions of Thiobismol ... sodium bismuth tartrate 2 c.c. (64 mg. Bi) or Iodobismitol 2 c.c. (50 mg. Bi) It can also be accomplished with weekly injections of oil-soluble Bismocymol 2 c.c. (100 mg. Bi) or Biliposol 3 c.c. (90 mg. Bi) It can be accomplished also with weekly injections of oil suspensions sodium potassium bismuth tartrate 1 c.c. (48 mg. o 64 mg. Bi) or bismuth salicylate 1 c.c. (123 mg metallic Bi) (Rollman et al. AmJS 21 480 506, 193 )

Bismuth is usually given intramuscularly. Sobisminol mass by mouth, produces urinary and fecal excretion figures which indicate that it should yield (?) antisyph little effects, and it does (Heininger and Barnett J 113 2214, 1939 AmJS 29 174 1945) Bistrimate orally is effective (Lehman and Parrett AmJS 31 640 194 ) Other effective bismuth preparations include the ... (Alexander and Schoch ADS 43 676, MRec 153 227 1941) the ethyl camphorat ... (Rusk and Silberstein 194 ) and the orally administered sodium bismuth triglycollamat (Sawicky JInvD 8 139 194 ) Bismarsen combines antisyphilitic properties of bismuth and arsenic and is of some popularity (Beerman et al J 120 333 194 )

Bismuth and lead are similarly metabolized Administration of bismuth may light up a latent plumbism (Epstein ADS 41 39 1940) and the mobilization and excretion of bismuth are enhanced by giving ammonium chloride (Brown et al. AmJS 27 301 1943)

One cannot rely upon bismuth ... the sole antisyphilitic drug (Walsh and Becker J 116 484 1941)

**Standardized Arsenical and Bismuth Treatment Schedules.**—The U S Army used a moderately intensive continuous schedule with Mapharsen twice weekly for 10 weeks, the first 5 weeks accompanied by bismuth subsalicylate weekly followed by 6 injections of bismuth at weekly intervals, followed by another 20 doses of Mapharsen in 10 weeks, the last 5 weeks being accompanied by bismuth. The total course of 40 doses of 0 06 gm Mapharsen and 16 doses of 0.2 gm. bismuth proved well tolerated and efficient. Sternberg and Leifer (AmJS 31 124 194 ) reviewed the data involving 400,000 soldiers, of whom only 6 died as a result of antisyphilitic therapy Of 3,000 cases of early syphilis results were satisfactory in 98 per cent of the seronegative cases, 94 per cent of the seropositive primaries, and 89.3 per cent of secondary There were 18 abnormal spinal fluids among the 2,442 examined. On a schedule of 20 injections of arsenical and bismuth given weekly Hood (AmJS 27 267 1943) reported involution of 84 4 per cent of early syphilis within 6 weeks, seronegativity in 84 6 per cent by the end of treatment followed by subsequent resolution

to a total of 90 9 per cent, and unsatisfactory outcome within a period of 33 months in 13 6 per cent in the classifications of resistance, relapse, and central nervous system involvement.

Regarding a schedule of 3 doses of arsenical per week in 4,623 cases of early and late syphilis, Eagle (J 126 538 1944) reported that toxicity interrupted the plan in 106 instances, and there were 4 deaths, all in females, young Negresses suffering most of the severe reactions. *Without bismuth the results were poor* When 9 doses *of bismuth accompanied* a total of 1,600 mg Mapharsen, treatment failures comprised only 9.3 per cent.

More rapid treatment, utilizing 20 mg Mapharsen per kg. body weight, divided into 20 equal doses on 20 consecutive days and accompanied by 1.28 gm. bismuth subsalicylate in oil was assayed by Pillsbury and Loveman (AmJS 31 115 1947) there was no death and in patients followed one year serologic relapse developed in 2 4 per cent of the seronegative primary cases, 5 6 per cent of seropositive primary and 4.6 per cent of secondary Spinal fluid abnormality was found in 6 of 785 cases They concluded that the method compared unfavorably with penicillin or penicillin combined with other chemotherapy

There is little doubt that penicillin in combination with other chemicals is better than penicillin alone and, while optimum therapy for human beings has not as yet been determined, it may well consist of penicillin Mapharsen, and bismuth in some combination (Eagle et al. VDI 27 3 1946)

**Iodides** have no specific action on the causative organism, but they provoke serous degeneration of granulation tissue and so aid in the healing of gummatous lesions. Perhaps also they open up new avenues of attack for the treponemicidal drugs. Potassium and sodium salts are commonly employed. Small doses of 0.3 to 1.0 gm. a day seem as efficient as large ones. Iodides are given by some therapists for the gentle treatment of late stages of the disease in the stimulation of resistance, in visceral and neurosyphilis and in the management of treatment resistance. Modern usage would limit the use of iodides to their administration in cases of cardiovascular syphilis in patients of 70 years or so of age (Moore)

**Mercury**.—The antisyphilitic efficiency of mercury is conditioned upon maintenance of an adequate concentration of diffusible dissociable mercury That which is fixed in the tissues plays no therapeutic role. Urinary excretion, not fecal, serves to indicate the diffusible mercury All effectual therapeutic methods show a continuous cumulative type of excretion. The daily urinary excretory level must be 10 mg of mercury to be effective this may cause stomatitis (Cole et al. ADS 19 105, 1929)

ORAL ADMINISTRATION is the simple method. This is especially indicated in visceral syphilis, when too rapid killing of spirochetes is to be avoided The protoiodide pill is often prescribed, 1/6 grain after each meal, gradually increased to 1/2 grain or even 1 grain until the physiologic effect is secured, as evidenced by slight tenderness of the gums, gastric disturbance and frequent bowel movements. Mercury with chalk is also popular

INUNCTION has been a valuable method of administration. The 33 per cent unguentum hydrargyri mite is the favorite preparation, 4 to 6 gm. to be applied once daily The drug is rubbed and massaged into nonhairy regions in turn, so that each area is used only once in 8 days, and irritation is not likely to ensue. Inunctions are given in courses, a series of daily treatments extending over a period of from a fortnight to a month, being alternated with similar periods during which some other form of antisyphilitic therapy may be administered. A series of 40 rubs is a course often prescribed

INJECTION supplies a convenient and efficient method of dosage Soluble or insoluble preparations may be employed. The injections are commonly made in the gluteal region. Colloidal mercury sulfide is recommended by Eakon and Jacobson (IIIMJ 76 172, 1939)

Soluble salts are efficient, but to maintain an adequate concentration of the ion, doses must be given at frequent intervals. The bichloride in doses of from 1/24 to 1/12 grain, the succinimide in doses of from 1/6 to 1/3 grain, or the biniodide or benzoate from 1/24 to 1/12 grain may be given once daily, or on alternate days. Mercuric salicylate, insoluble and suspended in a vegetable oil, is extensively used. The initial dose is 0.065 gm., and injections are made at intervals of 3 or 4 days.

℞ Mercuric salicylate,
Anesthesin ........................................of each 2.0
Wool fat ........................................ 4.0
Olive oil ........................................ 30.0
Mercuric salicylate ....................0.065 gm. per 1.0 c.c.
Label. Mercuric salicylate in oil, 0.065 gm. per 1.0 c.c.
Shake well and inject intramuscularly

The urine should be tested for albumin frequently during a course of injections of mercury which must be withheld if protein is present.

Bacitracin, 5,000 units per kg., cured rabbit syphilis in one dose (Eagle and Fleischman: PSExperM 68: 415 1948)

Penicillin.—Four cases of early seropositive syphilis were treated with the arbitrarily selected dose and time factors of 25 000 units each 4 hours for 8 days for a total of 1,200 000 units by Mahoney et al. (VDI 24 355, 1943 AmJPubH 33 1387 1943) with reversal of the dark field within 16 hours and of serologic reaction in 30 to 70 days. Herxheimer reactions occurred in all, and the clinical lesions healed with notable rapidity Since their report, syphilotherapy has undergone astonishing change.

Evaluation studies were kept orderly by Moore and his collaborators of the Penicillin Panel of the Subcommittee on Venereal Diseases of the Nation Research Council, who controlled the penicillin available for the treatment of syphilis when the supply was limited. With the end of war and the unlimited availability of pure penicillin, the most various therapeutic schemes have been and are being tested. One of Mahoney's original cases underwent a gradual serologic relapse and he and colleagues (J 126 63, 1944) were able to report results in 100 additional cases 2 instances of mild exfoliative dermatitis appeared, the average time for serologic reversal was 70 days, 7 patients underwent serologic relapse, and it appeared that as with arsenicals a certain proportion of patients fail to enjoy a curative response. The Penicillin Panel in a preliminary report (J 126 67 1944) showed that, on dosage schedules with totals ranging from 60 000 to 1,200 000 units, the relapse rate varied inversely with the dose, and that penicillin in combination with 320 mg Mapharsen a subcurative dose of the arsenical, gave the lowest relapse rate of the schemes tried. The excellent influence of penicillin was observed on meningovascular neurosyphilis, arsenical and bismuth resistance and congenital syphilis in infants. Stokes et al (J 126 73 1944) reported on the results in late syphilis, 122 cases of 182 being neural Gummas of skin and bone healed promptly Reagin was reduced in 50 to 60 per cent of all late cases. Patients seroresistant with previously employed treatment methods usually improved on penicillin Spinal fluid abnormalities improved in 74 per cent to at least some degree, the common change being a drop in cell count and total protein, so that fluids of low cell count showed comparatively little improvement Previous treatment for neurosyphilis by older methods, including fever therapy did not appear to prepare patients for superior results with penicillin These fundamental findings have been confirmed and elaborated by later studies.

The relapse rate in the 96 cases of early syphilis of Leifer (J 129 1247 1945) was 8 3 per cent Of 72 patients followed a year or more 70 were seronegative of 89 patients whose spinal fluids were examined 6 months or later following treatment, 86 were normal including 6 whose fluids were not normal prior to treatment.

The persisting problem of the best dosage and time schedule was elucidated by Eagle et al. (BullJHH 79 168 1946) who showed that in rabbit syphilis the greater the number of injections the less the total amount of penicillin required for cure, and that cure is favorably influenced by increasing the frequency and number of injections and the total dose. The minimum dose in human syphilis should be at least 2,400,000 units in 7.5 days with intervals of not more than 3 hours between injections (Schoch and Alexander J 130 696 1946) Barksdale (SMJ 39 229, 1946) stated, on the basis of the effectiveness of penicillin on dark field, serologic tests, healing of lesions, and improvement of spinal fluid abnormalities It is the best drug we have ever had in the treatment of syphilis. Relapse during penicillin therapy apparently occurred (Cole et al. OhioSMJ 42 59) 1946) and failures minimally of 15 per cent when the 2,400 000 unit dose was employed were recognized by the Committee on Medical Research and the U.S P.H S (J 131 265 1946)

The failure rate was higher in syphilis of longer duration. Reinfection certainly accounts for some failures, but no one knows precisely what proportion O Leary and Kierland (J 132 430 1946) summarized their evaluation by pointing to the few untoward reactions penicillin produces, the short time needed for its administration its excellent effect on cutaneous, osseous, gastric early hepatic and meningeal syphilis, and its particularly gratifying influence on the pregnant syphilitic woman, for whom it seldom fails to prevent the development of syphilis in the offspring The 2,400,000 unit schedule with 3-hour intervals between doses of 40 000 units yielded satisfactory results in 94 3 per cent of seronegative primary cases, 89.5 per cent of seropositive primary and 83 per cent of secondary while post treatment spinal fluid examination of 719 early cases showed abnormality in only 5 (Sternberg and Leifer J 133 1 1947) Results with 40 000 units each 2 hours for 85 injections and a total of 3 400 000 units were recorded in 728 cases by Arnold et al (JInvD 9 269 1947) no patient had to interrupt treatment because of reaction to the antibiotic and retreatment was required for only 17 of whom 14 showed clinical evidence of early syphilis which might have been reinfection while the remaining 3 were apparently true instances of serologic relapse or failure

Penicillin G is the most potent of the penicillins (Arnold et al. AmJS 31 469 1947) *Precocious tertiarism may follow inadequate dosage* (Marshall BMJ 2 612, 1947) Hyperpyrexia as well as combination with arsenicals and bismuth improves the therapeutic efficacy (Eagle et al AmJS 31 239 1947)

Evaluation is progressing regarding the use of daily injections of penicillin in oil and wax, escaping from the requirements of hospitalization and the 3-hourly needle Results are indeed hopeful for Thomas et al. (VDI 28 19 1947) found that there was no advantage of 2 injections daily over 1 that failure statistics were no worse than with any other type of rapid treatment and that as with other treatment schedules, most relapses or reinfections occurred during the first 6 months after treatment In their series of 802 patients given 600 000 units daily one group in 2 doses

of 300 000 units each, the other 600 000 units in one dose, for 8 days, only 2 patients had to discontinue therapy in both instances because of severe urticaria. A schedule of 8 injections of 300 000 units given in 8 days appeared satisfactory in 58 of 60 patients treated by Romansky and Rein (J 132 847 1946) Daily injections of 300 000 units in oil combined with 20 doses of arsenical and 5 of bismuth comprised the ambulatory scheme which seemed effective in the experience of Hazel (VDI 28 103 1947) The Council on Pharmacy (J 136 873 1948) approved 100 000 units each 3 hours or 600 000 units in wax daily for 10 days, and stated that no proof had as yet been obtained of the existence of a strain of *T pallidum* resistant to penicillin.

Since penicillin has become relatively inexpensive and since a patient is not overdosed by 100 000 units in saline each 3 hours, and since the addition to a treatment schedule of Mapharsen a relatively safe drug and bismuth enhances the likelihood of cure a plan of treatment we often use comprises 8 million units of penicillin given in 10 days of hospitalization 100 000 each 3 hours in saline, followed by 1.2 gm. of Mapharsen divided into 20 doses of 0 06 gm each given twice a week, and 10 doses of bismuth given once a week. We do not know whether patients so treated are over treated, but we are pretty confident that a patient who has received such treatment has received about all that chemotherapy holds for him If a satisfactory result has not been attained, fever therapy is indicated, unless the unsatisfactory result may reasonably be presumed to signify reinfection, which for therapeutic purposes, means starting over

The ill effects of penicillin are the dermatitis medicamentosa it can cause (p 107) and Herxheimer reactions, but intolerance is rarely a serious menace to the patient under treatment, wrote Thomas et al. (JInvD 10 77 1948)

**Heat in the Treatment of Syphilis**—MALARIAL THERAPY in chosen cases of neurosyphilis offers good chance of improvement See review of Simpson et al. (BJVD 17 1 1941) Wagner von Jauregg (1887) first noted its beneficial effects, and he began using inoculations systematically in the treatment of general paresis in 1917

To inoculate malaria, 5 cc of blood of a malarial patient is injected intravenously without cross matching, and 10 chills, more or less, are allowed to follow, if the patient tolerates the infection Quinine or quinacrine is then given in order to kill the plasmodia and stop the chills.

Malaria yields best results when given early in the course of neurosyphilis In asymptomatic neurosyphilis it was regarded as the best agent known for it prevented half the cases from becoming symptomatic and it succeeded sometimes after chemotherapeutic agents failed (O Leary J 110 42 1938) It fails in paresis due to prenatal syphilis The best outlook is in patients with out nervous system involvement who have a background of treatment, but improvement or failure does not parallel the spinal fluid complement fixation reaction (Wile and Hand AmJS 20 630, 1936)

Complications of malarial therapy include (1) fatality from cardiac or hepatic failure or from rupture of the spleen and (2) nonfatal difficulties, such as headache vomiting diarrhea, toxic psychosis, edema jaundice purpura herpes, etc. (Read et al. AnnIntM 24 444 1946; Roberts and Cara et AmJS 30 330 1946)

It is possible that a quartan strain may be preferable; it more frequently takes than tertian and is a milder disease although the incubation period and duration of infection are longer so that more hospital time is consumed (Kroll AmJS 4: 148, 1940) Chill may be regularized by single doses of Thio-bismol (Cole et al. J 115 422, 1940) although this is seldom necessary desirable after one has become intimate with the supervision of therapeutic malaria details of which are not given here. Deaths following malarial therapy were carefully investigated by Wile and Mundt (AmJS 26: 151, 1942)

FOREIGN PROTEIN THERAPY may favorably influence the course of syphilis as an accessory measure, especially in resistant cases and in interstitial keratitis. The effect is at least in part due to fever

HYPERPYREXIA MAY BE PRODUCED ARTIFICIALLY by foreign proteins such as intravenous typhoid injections (Nelson OklaSMAJ 27 87 1934 Laurence AmJS 28 289 1944 Smith et al. SMJ 38 194, 1945) hot baths electric blankets, radiant heat, and high frequency radio waves.

In any method, a temperature approximating 105 F rectally maintained for 4 hours is to be attained. This may be repeated on alternate days o twice a week for 10 treatments. The means for obtaining it are not important of themselves, and artificial fever is probably as effective as malaria (Simpson et al. VDI suppl. 16, 1942) The costs are less, the convenience and control greater the hazards in expert hands fewer (Simpson et al. BJVD 17: 1, 1941)

The infrared cabinet is safest.

Administration of therapeutic pyrexia demands the undivided attention of an experienced physician and a skilled nurse as well as adequate apparatus.

Artificial hyperpyrexia is well tolerated by patients with normal hearts, kidneys, and blood vessels, and is contraindicated by age over 60 years, cardiac or renal insufficiency advanced arteriosclerosis, pulmonary tuberculosis, and late neglected dementia of neurosyphilis.

Complications of heat therapy include burns and vesicles, nausea and vomiting, usually commencing toward the end of a treatment, controlled by oxygen inhalation and by intravenous injection of 1,000 c.c. of 10 per cent glucose; herpes labialis; tetany due to acidosis and hyperventilation, controlled by calcium gluconate intravenously or by carbon dioxide i halations. An occasional patient put into the hot box rises in temperature abruptly extremely and with fatal outcome in spite of everything done toward his rescue. Such a possibility can be prevented *only by the utmost diligence in supervising the treatment, for* if the temperature shoots up the emergency must be recognized at once. Salt loss, too, is a danger; a gram 3 times a day should be given throughout the course of fever therapy in all cases.

Fever alone will render the darkfield negative in 94 per cent of primary lesions and produce recessions of secondary eruptions, but it will not alter the positive blood test. Fever alone is inadequate (Simpson et al. AnnIntM 7 64, 1933)

Fever therapy is indicated in all cases of neurosyphilis, unless contraindicated by the patient s estimated inability to withstand it. Until penicillin therapy of meningovascular syphilis has been further evaluated—and it is true that penicillin alone may prove to be adequate in at least some cases (Gammon et al. J 128 653, 1945 O'Leary et al.: ib. 130 698, 1946 Stokes et al. ib 131 1 1946 Moore and Mohr AmJS 30 405 1946 Heyman AmJMSc 213 661, 1947 Leavitt ADS 56 233, 1947)—one is tempted to say that neurosyphilis has not been treated adequately until fever as well as chemotherapy has been utilized see p 280

**Combined Therapy**—In primary and secondary infections, the use of fever combined with chemotherapy is experimental (Kendell et al. APhysM 26 76 1945) The combination of fever therapy with chemotherapy has seemed to be advantageous, however apparently yielding better results than chemotherapy alone in early stages of syphilis as well as in late (Beckh and Barnett AIntM 63 974 1939) Fever is used almost routinely in neurosyphilis (q v ) where various combinations with chemotherapy have been evaluated. Adequate treatment with arsenicals and bismuth has been assessed as yielding when used auxiliary to fever at least twice the spinal fluid reversal rate of fever alone (O'Leary et al. J 115 677 1940) Combinations of penicillin with fever therapy are especially promising (Curtis et al. AmJS 31 618, 1947)

It is standard practice to use more than one agent in syphilotherapy wherein treatment plans involving arsenicals and bismuth, penicillin and arsenic and bismuth, or fever with these, are modern science, while the exhibition of mercurials and iodides in conjunction with these might be classed as art. Multiple attack upon the infection is empirically known to be effective, the agents used being divisible into the spirochetocides and the resistance-builders. Fever therapy could be called the final resort in difficult cases exemplified by neurosyphilis, resistant syphilis, interstitial keratitis and optic atrophy. However when it is correct to use fever therapy at all, it is usually correct, or even urgent, to use it promptly rather than hesitantly and belatedly after irremediable damage has been done. In the most difficult imaginable case of syphilis, with reservations regarding cardiovascular or hepatic damage disastrous to the victim, the patient may be said to have received everything when he has received adequate penicillin, arsenical, bismuth, and fever therapy and when all foci of infection have been eradicated and all detectable debilitating adjunctive conditions have received the attention they deserve. There comes a time when one can do no more; nothing is gained by flailing a dead horse.

**Duration of Treatment.**—It was once thought proved that even with modern methods of treatment, few cases of syphilis are cured before the end of 1 year and that the majority require at least 2 years of active medication. American practice sustained by evidence collated by the Cooperative Clinical Group insisted on the continuous method of treatment, with no rest periods. If no clinical evidence of the disease was to be found after 18 months of treatment, a 6 months vacation from medication was taken, then serologic tests were made. Titered estimations are particularly instructive. If examination still proves negative, a further rest of 6 months is taken, provided always that no relapse is manifested, and a second examination is made. If still negative, a further rest of 6 months, and a third test. A year later a final examination is made. If any of the analyses are positive, treatment is reinstituted.

With speedier methods of treatment, the old standards have required revision. Following a treatment period ranging from a few days to a few weeks in duration, titered serologic tests should be made monthly for a year then at lengthening intervals. If the serologic titer remains zero or low and if the spinal fluid remains normal or of inactive formula, and if the cardiovascular examination including fluoroscopy is normal and if 5 years have elapsed since the termination of treatment, the patient may with considerable security be judged cured.

Spinal fluid is often abnormal when the blood ceases to show evidence of the disease. Asymptomatic neurosyphilis is a great danger to the patient, for it is manifested by no abnormality whatever in the clinical examination yet presages progressive neurosyphilis and the worst results that syphilis produces. *In every instance* it is necessary to examine the spinal fluid.

**Latent Syphilis.**—Patients who have clinically nonrecognizable syphilitic infection the blood serologically positive and the spinal fluid normal, fall in this class. If no previous treatment has been given, or if previous treatment has been inadequate then treatment should be given in order to decrease the probability of clinical progression or relapse. Cooperative Clinical Group studies have shown that without treatment the outcome over a period of years is favorable in 35 per cent but with proper

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In any method a temperature approximating 10₆ F rectally maintained for 4 hours is to be attained. This may be repeated on alternate days or twice a week for 10 treatments. The means for obtaining it are not important of themselves, and artificial fever is probably as effective as malaria (Simpson et al. VDI suppl 16, 194 ) The costs are less, the convenience and co trol greater the hazards in expert hands fewer (Simpson et al.: BJVD 17: 1 1941)

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Verifiable osteitis in early syphilis is rare and quite similar to that occurring commonly in late benign syphilis (Reynolds and Wasserman AIntM 69 263, 1942). The skull is the usual site especially the frontal, parietal, and nasopalatine bones; the sternoclavicular site is next in frequency and the long bones last. Pain and local tumor respond well to specific treatment, penicillin being notably effective (Naffziger et al: J 131 1183, 1946). See also congenital syphilis of bones.

**Visceral Syphilis.**—The lung may be affected in late benign syphilis, roentgenograms showing localized shadows or a more widespread process. It is rare, and it responds as a rule quite satisfactorily to specific therapy including penicillin (Kulchar and Windholz AmJS 31 166 1947).

Affecting the kidney early syphilis occasionally induces a nephrosis in which the urine is grossly abnormal but function tests are not much altered. Early syphilitic nephropathies heal promptly under intensive specific therapy and leave no sequelae (Thomas and Schur AIntM 78 679 1946; Scott and Clark AmJS 30 463 1946).

The liver is commonly affected with late benign lesions of the tertiary sort. Hepatic gummas destroy blood vessels and induce fibrosis. Resolution is followed by deep and extensive scarring. The dense scars are generally stellate and deforming and the organ may be subdivided into lobes, hepar lobatum. Patients may be asymptomatic or may have an upper abdominal tumor usually firm, with low fever attributable to necrosis within the gummata or there may be slight icterus, epigastric pain and tenderness, and ascites simulating portal cirrhosis. The liver may be smooth because the nodules are within it, or it may be nodular with palpable, firm tumors. Jaundice during antisyphilitic therapy is a confusing finding for arsenical intoxication may induce it, and infectious hepatitis may occur especially if the virus thereof is inoculated in a treatment clinic by a break of aseptic technic (Mitchell CanadMAJ 48 94 1943; Anderson BJVD 19 58, 1943). It apparently is safe to continue bismuth therapy during such jaundice (Forbes BMJ 2 852, 1944). Yet syphilitic hepatitis in early syphilis responds satisfactorily to arsenicals, according to Leonard (AmJMSc 208 461 1944) who reported a death from acute yellow atrophy in a jaundiced girl with the secondary rash who had a Herxheimer reaction following the first dose and thereafter became more jaundiced. When late syphilis of the liver is symptomatic excellent improvement followed the use of penicillin in the patients reported by Tucker and Dexter (AIntM 58 313 1946). Hepatic syphilis was well reviewed by Hahn (AmJS 27 529 1943).

Gummatous involvement of the stomach is rare and is difficult to distinguish from peptic ulcer but it is responsive to specific treatment although deformity may require surgical intervention.

**Cardiovascular Syphilis** designates the practical concept of syphilis of the aorta with the cardiac changes secondary thereto (Kampmeier Essentials of Syphilology Lippincott 1943).

Diffuse myocarditis occurs and is clinically manifested by impaired myocardial function, with palpitation, *precordial discomfort* and dyspnea on *exertion*, *possibly failure*. Diagnosis is by exclusion of other possible causes in an inadequately treated syphilitic patient (Mattman and Moore [illegible] 711 1943). Gumma may occur in the myocardium, giving evidences of its existence dependent on its location and size.

Aortitis is the common cardiovascular lesion. While invasion of aortic tissues occurs early probably clinical manifestations develop only after some years. The pathologic lesion is the usual perivascular one the vasa vasorum being affected and the wall of the great vessel thereby weakened, scarred, and allowed to dilate (Hower

AmJS 27: 50, 1943) The intima shows longitudinal creases or striation, thickened patches of bluish-gray overlying active disease subsequently to be replaced by depressed scars. The aorta becomes dilated and lengthened and, since the root of this vessel is the usual site of the process, dilation of the aortic ring occurs, with separation of the valve leaflets, and aortic insufficiency as a result. The valves themselves may be involved so that their edges become rolled and thickened. The orifices of the coronary arteries may suffer. Thus, by degrees and extent of involvement and by location of the pathologic process, the results of syphilis of the aorta are classed as uncomplicated aortitis, aortic insufficiency and aneurysm.

Necropsy studies of aortas from 45 syphilitics who had and who had not received adequate antisyphilitic treatment showed that few of the former but all of the latter group had histologic lesions of active syphilitic aortitis (Webster and Reader: AmJS 32: 19, 1948)

Details of the internal medical aspects of these variations of cardiovascular syphilis will be found in such texts and Moore's and Stokes's. Cardiovascular syphilis is largely preventable by adequate treatment of early syphilis (Thompson et al AmHJ 17: 286 1940) If insufficiency decompensation develops, the prognosis is bad indeed. Rupture of the aorta is a likely and dramatic termination of the case in a syphilitic with aneurysm.

The Cooperative Group (Cole et al. J 108: 1861 1937) reported as follows: Of the approximately 500 000 syphilitics in the United States who seek treatment for the first time late in the course of their disease about 50,000 have detectable cardiovascular syphilis. Of this type of involvement, 7 per cent occurs within 5 years of the initial infection it is late in onset. Best treatment is prophylaxis. The disease must be treated gently to avoid therapeutic paradox. Uncomplicated syphilitic aortitis is present in 4.9 per cent of patients with latent or late syphilis. It is 3 times as common in the Negro as in white persons. The Wassermann test is positive in 7° per cent and the spinal fluid is abnormal in 49 per cent of the cases. Of 933 patients with early syphilis followed 3 to 10 years, 1.6 per cent developed cardiovascular involvement of 105 followed 10 to 20 years, 6. per cent developed it. In the 3- to 10-year group, not one developed cardiovascular disease if he had been adequately and regularly treated in the early stages of the infection. If aortitis is clinically evident, treatment improves the outlook more than doubling the expectancy. Start with a course of metal and use small doses. Aortic regurgitation is seen most often after 20 to 30 years and is associated in 63 per cent with spinal fluid abnormality. In it 60 per cent had had no previous antisyphilitic therapy and in the remainder treatment had been given irregularly and late. The average length of life if cardiac failure was present before treatment began was 20 months if not in failure 4 months. In 4 cases of aneurysm, 50 per cent of those of the saccular type occurred in patients 15 to 25 years after infection. Wassermann tests were positive in 90 per cent, spinal fluid abnormality in 64 per cent and 31 per cent were associated with clinical neurosyphilis. No treatment had been received by 77 per cent. Symptomatic relief was obtained through treatment in 44 per cent those inadequately treated lived on an average 37 months after diagnosis, while those adequately treated lived 75 months.

In the treatment of cardiovascular syphilis, the objective is to induce slow rather than abrupt resolution, avoiding Herxheimer reaction and therapeutic paradox. Long preparation with bismuth, mercury and iodides has been the practice. Penicillin is effective in inducing healing of active lesions after suitable preparatory treatment, but nothing can cure a scar. T ker and Turner (AIntM 80 3—, 1947) gave full doses of penicillin at once and did not see severe reactions, the dangers of which they judged had been overrated

**Ocular Syphilis.**—The conjunctiva may be the site of the primary sore. Iritis occurs in perhaps 4 per cent of cases of early syphilis, chorioretinitis is uncommon but occurs in the late secondary stage uveitis with secondary keratitis in late acquired syphilis carries a serious prognosis (Woods AmJS 27 133 1943) See neurosyphilis regarding optic atrophy (p 283) congenital syphilis regarding interstitial keratitis (p 290)

**Neurosyphilis.**—The central nervous system is invaded early in the course of the infection Abnormal spinal fluids were disclosed by Cooperative Clinical Group investigations (VDI 18 45 1937) in 25 per cent of seronegative primary 30 per cent of seropositive primary and 33 per cent of early secondary cases. Abnormality may not be noted with stand

ard methods of testing for inoculations into rabbits of apparently normal spinal fluid from patients with early syphilis gave positive results in 14 per cent of the fluids tested by Chesney and Kemp (J 83 1725 1924) Despite the high frequency of spinal fluid evidence of neurosyphilis in early cases, clinical neurosyphilitic manifestations develop in a considerably smaller proportion of untreated patients, estimated at from 5 to 10 per cent. There is no doubt that self healing occurs in many instances. Adequate treatment in early syphilis reduces the probability of clinical neurosyphilis to 1 or 2 per cent (Moore) but inadequate or irregular treatment are followed by higher rates of incidence. If the spinal fluid remains normal for 4 years after infection, the development of neurosyphilis is extremely unlikely

The diagnosis of neurosyphilis rests primarily on spinal fluid examination. The one spinal fluid test, of the several which standardly should be employed, which is diagnostic of syphilis is the complement fixation test, precipitation reactions being little used and less reliable.

Misleadingly Positive Wassermann reactions are indeed exceptional, although they have been reported in some cases of meningitis, tuberculous, meningococcic, and lymphocytic (Scott et al.: AmJS 28 431, 1944)

The Complement Fixation Test must be done in several dilutions, standardly 1.0, 0.5, 0.25, and 0.1 c.c. It is an error to omit the 1.0 c.c. dilution, for many cases are found to be positive with 1.0 c.c. yet negative in 0.5. It is desirable to titer the test to a negative reaction so that a base line may be attained for comparison with later findings. If positivity is found at 0.1 c.c., one desires to know the result with 0.05, which is not rarely positive, and with 0.025. A change between consecutive spinal fluid examinations of only 1 dilution may not be significant, but if positivity is found at 0.1 c.c. at one time and later at 0.5, with 0.25 negative, improvement may be estimated to have occurred.

Other Spinal Fluid Tests are the cell count with differentiation of the varieties of cells, a qualitative test for globulin, the total protein in mg./100 c.c., and the colloidal gold or mastic test. Interpretation of the significance of spinal fluid findings has been clarified by Dattner and Thomas (AmJS 26: 21, 1942) and by Dattner (Neurosyphilis, Grune and Stratton, 1944)

Activity of Disease is indicated especially by increased cell count, particularly when a high proportion of the cells are polymorphonuclear leucocytes, and by increased protein. In general the colloidal curve, a set of digits ranging from 0 to 5 and indicative of the intensity with which the colloid is influenced by serial dilutions of the spinal fluid, parallels the globulin content. Results are reported as 0000000000, negative 5555421100 (for example) "first zone" or "paretic type" implying the presence of much globulin, or 0012321000 (for example) "syphilitic" or "mid zone," suggestive of less intense reaction. Gold curves help in evaluating the fluid, but are the least significant part of the complete report. When under treatment a series of such curves are obtained and the 5' drop out, improvement may be interpreted but many conditions other than syphilis, such as meningitis, myxedema, and bloody fluid also give rise to abnormal gold curves (Merritt and Fremont-Smith Cerebrospinal Fluid, Saunders, 1938) The presence of globulin found by the Pandy or Nonne-Apelt test is abnormal, but not diagnostic of syphilis. Total protein ought to be 40 mg per cent or less and is often about 20 in normal fluids, but is elevated by any kind of meningeal irritation. The cells of the spinal fluid are especially significant, and 0 or 1 or 2 lymphocytes per cubic millimeter are clearly normal, while 10 WBC is certainly not normal. The exact number of cells to be interpreted as normal or abnormal cannot be given, but 5 is a commonly quoted dividing figure. We have often seen neurosyphilis develop when the spinal fluid shortly after an "adequate" course of Mapharsen and bismuth showed 4 or 5 WBC and cases of neurosyphilis would have been picked up by a Wassermann using 1.0 c.c., proceeding always to be requested of the laboratory. When the cell count is high and contains numerous polymorphonuclear leucocytes, activity is great. Counts of 100 200 or more WBC are found in untreated meningovascular syphilis. The count drops rapidly under effective treatment. Low counts are usual in parenchymatous syphilis of the nervous system. The last abnormality to disappear when treatment of neurosyphilis is effective is usually the complement fixation test. Some fluids retain Wassermann positivity as a manifestation of neurosyphilitic latency when all other abnormality has dissipated.

Spinal fluid studies are almost sufficient of themselves in judging the requirement for further treatment (Dattner) If the formula becomes favorable, with diminution of complement fixation titer return of cell count and total protein estimations to within normal limits, and improvement in the colloidal test, and if the formula remains so without relapsing, further treatment is unnecessary. The spinal fluid cannot be induced to become entirely normal in all patients, by any means, although this is sought and prized if attainable (Thomas and [illegible] AmJS 29 467 1945)

Spinal Fluid Is to Be Examined in every patient with syphilis at some time during the course of his disease. The examination is not necessary in patients with fresh primary or secondary syphilis until they have undergone a course of adequate treatment, for this suffices to clear the spinal fluid in a high proportion of the early cases associated with abnormal fluids. After the administration of adequate treatment in early syphilis, we believe it wise to wait a month or two to do the tap, so that one

can evaluate the spinal fluid formula when it is not being depressed toward normal by intensive therapy. In latent syphilis not diagnosed until, say, 2 years or more have elapsed since inoculation, and in cases in which the date of infection is not known, spinal fluid examination correctly precedes the institution of antisyphilitic treatment as a necessary preliminary evaluation measure. This enables the physician to know whether he is dealing with neurosyphilis or latent syphilis, the distinction being of fundamental importance.

It is further essential to know with what type of neurosyphilis the patient is suffering. In only half the cases of neurosyphilis which occurred in the military personnel studied by Scheris and Caravati (AmJM 30: 330, 1948) was a trustworthy history of the approximate date of infection obtainable. A high proportion of persons suffering with neurosyphilis are unaware that they ever had syphilis and are unaware that there is anything at all the matter with them. Of those patients of Scheris and Caravati who manifested any detectable clinical abnormality and who were therefore classed as cases of symptomatic neurosyphilis, 66 per cent had ocular abnormalities, and 35 per cent of these had abnormal pupils. The incidence of ocular abnormalities increased as the duration of syphilitic infection increased. Competent ocular examination is a necessity in evaluating a case of neurosyphilis, and includes the estimation of the visual field which may be reduced as the first indication of syphilitic damage of cranial nerves.

SPINAL PUNCTURE may be represented as a safe office procedure, is extremely simple in expert hands, and does not require that the patient be kept horizontal for more than a few minutes after withdrawing the sample. A mild sedative given beforehand is helpful. The apprehensive patient suffers out of proportion to the amount he is hurt, which should not be much. The patient can usually be induced to submit to puncture if it is pointed out to him that there is no other way of ascertaining the state of his nervous system, which, for all he or a physician can know, is headed for disaster unless the facts are disclosed in this way. The cisternal puncture is recommended by some authorities.

*When the specimen is in the test tubes, the cell count should be determined at once.*

If the spinal fluid is found abnormal, repeated examinations for evaluating the effects of subsequent treatment are necessary. Each 3 months for the first year is not too much to ask of the patient, whose feelings must be considered but whose ultimate welfare must not be frittered away because of his reluctance to do what may reasonably be asked of him. If the spinal fluid is negative in a patient who has had syphilis for 4 years, further spinal punctures are not necessary.

When seroresistance or relapse is encountered following adequate treatment of early syphilis, the spinal fluid must be examined, even if a previous spinal fluid examination was reported negative.

ILL EFFECTS OF SPINAL FLUID EXAMINATION are trivial in comparison with the value of information so obtainable. About 20 per cent of those who undergo the procedure suffer more or less consequential postpuncture headache. This can be incapacitating for as long as a week, is relieved solely by lying down, may come on 1 day after the puncture, starts with stiffness of the neck and occipital aching and may be limited to these mild manifestations, is to some extent preventable by using narrow gauge needles (Dattner) and is probably due to meningeal irritation which is less likely to be annoying to persons whose syphilis has already produced meningeal irritation.

THE CENTRAL NERVOUS SYSTEM is derived from mesodermal and ectodermal tissues. When syphilis primarily inflames the mesodermal meninges and blood vessels, it is called meningovascular. When it primarily degenerates the parenchymatous ectodermal tissues, it is manifested as paresis if the brain is particularly affected, as tabes dorsalis if the spinal cord especially suffers, or as taboparesis if both are involved. Admixtures of these types of involvement are usual, although acute meningovascular syphilis may produce only the central nervous system manifestations of irritation and toxic psychosis, both of which disappear entirely when treatment is successful. Tabes dorsalis may be present though inactive when the spinal fluid is entirely normal. Among untreated syphilitics, about 5 per cent may be expected to develop paresis and 15 per cent meningovascular syphilis (Moore). Persistently positive blood tests were associated in 74 per cent of the instances with spinal fluid abnormality in the Cooperative Clinical Group material. But serofastness was not necessarily an attribute of asymptomatic neurosyphilis, for in about one third of the cases of early asymptomatic neurosyphilis under treatment the blood became negative, yet there was a great tendency for these cases to relapse. About 40 per cent of late asymptomatic neurosyphilis showed negative blood tests, so that the fact which deserves emphasis is that negative blood tests in treated syphilitic patients do not rule out the possible existence of neurosyphilis (Kampmeier).

THE VARIETIES OF NEUROSYPHILIS are classified as asymptomatic, wherein no clinical indication of neurosyphilis can be detected excepting the presence of abnormal spinal fluid; and symptomatic, wherein various abnormalities detectable by clinical examination are present in addition to abnormality of the spinal fluid. The following descriptions of these are condensed from O'Leary, Moore, Solomon, Stokes, and Thomas (Bull U S AMD Sept, Oct, Nov 1944).

**Asymptomatic Neurosyphilis** is characterized by abnormal spinal fluid findings, but there are neither physical signs nor subjective symptoms of invasion or involvement of the central nervous system. When a patient manifests clinical symptoms or signs which denote that the infection has involved the central nervous system, a diagnosis of

symptomatic neurosyphilis is no longer tenable. Asymptomatic neurosyphilis may be encountered in any phase of syphilis. It is noted most frequently in early syphilis in which the incidence approximates 30 per cent under older methods of treatment. The rate is much lower than this among well-treated patients. The rate among those untreated or those who have not had good modern treatment for acute syphilis gradually decreases until it reaches an average of 15 per cent of patients in whom the infection is more than 4 years' duration.

*Asymptomatic neurosyphilis is the forerunner of clinical neurosyphilis* but it frequently responds comparatively satisfactorily to treatment so that the development of clinical neurosyphilis is prevented. The results of repeated examinations of the spinal fluid are the only indicators of the response that the patient is making to treatment. They also denote the trend of the disease in the central nervous system, revealing the tendency for the fluid to change to the mild or to the severe (paretic) type.

*The significance of each test employed* in the examination of the spinal fluid must be understood in order to interpret the results of each test intelligently in terms of therapeutic effect and prognosis. Among patients who have asymptomatic neurosyphilis, the earlier in the course of treatment the spinal fluid is examined, the easier it will be to interpret the subsequent changes in the various tests, thus observing the trend and response of the spinal fluid to treatment. Re-examinations of the spinal fluid must be done at intervals of about 6 months if the significance of the changes in the abnormalities of the spinal fluid is to be interpreted accurately.

**Classification of spinal fluids according to the degree of abnormality observed on examination by each of the 5 standard tests**

| GROUP | CELLS PER C. C. | COLLOIDAL GOLD | SEROLOGIC REACTION | GLOBULIN | PROTEIN MG PER CENT |
|---|---|---|---|---|---|
| Group I (mild) | 5 to 20 | 0000000000 to 0012210000 | Negative | Negative or positive | 25-60 |
| Group II (moderate) | 20-100 | 0012240000 to 0124542000 | Doubtful or positive | Positive | 40-100 |
| Group III (severe) | 10-100 | 5555543210 | Strongly positive | Positive | 75-150 |

"Mild" includes fluids in which the number of cells and content of globulin and protein may be increased, the complement-fixation reaction negative in 0.5 c.c., and the colloidal curve may be indeterminate or positive. If positive the curve is usually of the syphilitic zone type.

"Moderate" includes fluids in which the cells number 20 or more per c.c., the complement-fixation reaction is positive or strongly positive, and the colloidal curve is of the tabetic or indeterminate type. The estimate of the globulin is positive and the estimate of protein shows an increase to an average of 60 mg. per 100 c.c. [illegible] is falling just short of the requirements of the severe group are also included in this group.

"Severe" includes those fluids that have the "paretic formula," that is, marked excess of globulin, content of protein averaging about 100 mg. per 100 c.c., a strongly positive complement-fixation reaction (0.2 c.c. or less) and the type of colloidal curves indicating dementia paralytica. The number of cells is decidedly increased. In addition to small lymphocytes, large lymphocytes and polymorphonuclear leukocytes may be present.

It is possible to recognize from the spinal fluid findings that different types of neurosyphilis are impending. It is not possible to make such deductions from one, but rather from successive examinations of the spinal fluid. For example, in a case of asymptomatic neurosyphilis, the paretic type of formula may be reported in the spinal fluid at the time of the first examination. If after 6 months of treatment, the paretic features of the fluid persist this finding then assumes significant proportions. If this paretic formula remains, it is convincing evidence that the patient has a resistant type of infection, that the treatment given him has been inadequate, and that a change of the therapeutic program is warranted. On the other hand some patients who have asymptomatic neurosyphilis may affect a paretic trend in the original test of the spinal fluid, but after 6 months of treatment no longer have the paretic features in the spinal fluid; in these negative results may be obtained after the second period of 6 months of treatment. If the trend of change in the fluid is from the group III toward the less severe types of involvement, the inference is that the program of treatment is probably adequate. If the group III features persist, or if the fluid relapses toward the severe type after a rest from treatment, a change of the therapeutic program should be considered. Patients who have severe and persistent abnormalities of the spinal fluid deserve neuropsychiatric examinations at least every 3 months.

*Results of treatment* are best in the cases of asymptomatic neurosyphilis in which the abnormalities of the spinal fluid are the least severe and in those in which the patient has had the disease for only a short time. Results of chemotherapy are best in early asymptomatic neurosyphilis in which syphilis has been present for 2 years or less. When the disease has been present longer chemotherapy is frequently not capable of reversing the spinal fluid findings to normal. In such cases the early use of fever therapy is indicated. When the group III formula is encountered in examination of the spinal fluid, it is usually necessary immediately to adopt fever therapy and frequently to employ chemotherapy after fever therapy in order to reverse the reactions to negative. (See [illegible] et al., [illegible] 1940) on prognosis in asymptomatic neurosyphilis.

*Arrest spontaneously* occurs spontaneously in some cases of asymptomatic neurosyphilis. Although the incidence of these cases is not known, they are encountered

often enough to emphasize the fact that the forces of immunity of certain patients are mustered early in the course of the disease without the aid of treatment and overcome the invasion of the nervous system completely. The development of an immune response plus modern treatment prevents clinical neurosyphilis in a high proportion of cases.

*The treatment of asymptomatic neurosyphilis* varies, depending on the duration of syphilis, the type of the spinal fluid pattern, and the amount and type of treatment the patient has received previously. Best therapeutic results are observed in those who have had syphilis 2 years or less and who have the mild or moderate type (group I or II) of spinal fluid pattern, while less favorable results, as evidenced by clinical progression of the disease or persistence of the positive reactions of the spinal fluid or both, are noted in patients who have had syphilis for 4 years or more, who have the severe type (grade III) of spinal fluid, and who as a rule have had less than the minimal required amount of treatment during the early phase of the infection. Whatever treatment system is employed, its results should be checked by re-examinations of the spinal fluid at intervals not greater than 6 months.

Observation for 20 years of a group of patients with asymptomatic neurosyphilis and a study of their clinical progressions toward various types of clinical neurosyphilis indicate that the patients who had mildly positive spinal fluids showed the lowest incidence of clinical progression. Those who had the "paretic" formula in the spinal fluid gave evidence of the clinical progression more than 4 times as frequently. In the study of the influence of the amount of treatment, it was found that those who received less than 10 injections of an arsphenamine showed an incidence of clinical progression 3 times greater than those who received more than 20 injections of an arsenical preparation and a heavy metal. Even if modern treatment of syphilis does not "cure" in all cases, it decreases materially the incidence of late complications.

*Symptomatic Neurosyphilis.*—The symptoms of syphilis of the nervous system may simulate any variety of neuropsychiatric disorder. In disorders suggesting organic involvement of the nervous system, whether the symptoms or signs be physical or mental, neurosyphilis must be ruled out. Before making the diagnosis of neurosyphilis, all physical and psychogenic factors which may be of etiologic importance must be carefully evaluated. As syphilis gives no immunity to other diseases, the coincidence of 2 disorders is always possible.

*The pathologic response of the tissues* of mesodermal origin to the invasion of the spirochetes is a chronic inflammatory and proliferative reaction similar to that found in the skin and viscera. The nerve cells respond only by neurobiosis, and the neuroglia cells increase in number either as a reaction to the invasion of the spirochetes or as a type of replacement scar tissue when neurons have been eliminated. The difference in pathologic response and the fact that syphilis of the meninges and blood vessels rarely spreads to the underlying or surrounding nervous structure permit the division of cases of neurosyphilis into meningovascular and parenchymatous types. The clinical distinction between these is important, for cases of meningovascular neurosyphilis suffer little or no irreparable damage to nerve cells except secondarily by interruption of blood supply and are much more beneficially affected by trivalent arsenicals and bismuth than cases of parenchymatous neurosyphilis.

*The symptoms of neurosyphilis* are directly dependent on the locus of involvement and the extent of the lesion. Theoretically one should be able with careful evaluation to localize correctly the portion of the nervous system involved, but this is not always possible clinically. In a pure meningeal invasion, involvement may be limited to a small portion of either the spinal or intracranial meninges, or it may be widespread. The involvement may be primarily spinal, at the base of the brain, in the meninges over the vertex of the cerebrum, or confined to an even more limited area. Meningeal inflammation may be slight or extremely extensive, with proliferation in circumscribed areas leading to local pressure. The symptoms, therefore, of meningeal neurosyphilis depend on what nervous structures are secondarily involved because of the close juxtaposition of these tissues to the meningeal inflammation, as well as on whether vascular thrombosis has occurred. A marked inflammatory reaction in the meninges surrounding the thoracic spinal cord may strangulate the cord and cause the symptoms of cord transection. Involvement of the meninges at the base of the brain may lead to involvement of the cerebral nerves as they pass through the pia-arachnoid, causing extraocular muscle palsies, facial paralysis, or interference with function of other nerves. An inflammatory process which interferes with the outflow of cerebrospinal fluid through the basal foramina will produce increased intracranial pressure with all the symptoms and signs incident thereto. The meninges over the vertex may become so thickened as to produce focal or general pressure signs. If focal pressure occurs over the central area of the brain, convulsive seizures may ensue. Involvement of the blood vessels by the syphilitic process may cause damage to any vessel supplying the nervous system. If thrombosis results, the necessary blood supply will be cut off and nerve cell destruction may result. As practically any vessel may be damaged, leading to thrombosis and perhaps occasionally to rupture, every known syndrome of nervous system disease or disorder may develop.

*Parenchymatous neurosyphilis* is due to the invasion of the nervous tissue by the spirochetes and may show any type of symptoms producible by injury or destruction of nerve cells. The symptoms are either psychiatric or neurologic, or both. In the majority of cerebral cases the frontal lobes are predominantly involved, giving rise to the syndrome of general paresis. In the cord, the posterior roots and posterior columns of the thoracolumbar cord are most commonly involved, producing the clinical picture of tabes dorsalis.

*The clinical manifestations of neurosyphilis* may be classified under the following main headings: (1) meningeal neurosyphilis; (2) meningovascular neurosyphilis; (3) tabetic neurosyphilis; (4) paretic neurosyphilis; (5) vascular neurosyphilis; (6) congenital neurosyphilis; (7) various relatively rare and controversial syndromes, such as chronic anterior poliomyelitis, parkinsonism, and disseminated sclerosis-like pictures, not here described.

*Syphilitic Meningitis.*—Meningeal neurosyphilis may be either acute or chronic. Acute meningeal neurosyphilis usually occurs in the first 2 years of the syphilitic in-

fection. In the early stage of syphilis the meninges frequently show an inflammatory reaction. In most cases, recovery is either spontaneous or a result of routine treatment, but occasionally there occurs the syndrome of acute meningitis of a fulminating type. This is characterized symptomatically by a picture reminiscent of meningococcus meningitis, with fever, headache, stiff neck, and Kernig's sign. The spinal fluid may show pleocytosis up to 1,000 or more cells, 40 per cent of which may be polymorphonuclear leucocytes. In most cases the meningitis is of a much lower grade with less marked symptoms consisting mostly of headache, dizziness, and malaise. The cell count may be normal or as high as 100 to 200 cells.

*Acute syphilitic meningitis* is relatively rare but probably is seen most frequently in individuals who have had a few arsenical injections and then lapsed from treatment. The response to modern antisyphilitic treatment is usually prompt and satisfactory. In acute meningitis, globulin and total protein of the spinal fluid may or may not be greatly increased. The colloidal tests may be of any variety and the complement fixation or flocculation tests may be either strongly positive or more rarely negative.

*Chronic syphilitic meningitis* may occur at any time in late syphilis, but in most instances symptoms arise within 5 years of the original infection, although they may be encountered after more than 20 years. Trauma is occasionally an apparent precipitating factor in the development of symptoms. Symptoms may be of many types depending on localization and extent of the lesion. Among the syndromes encountered are the following:

(1) *Meningitis of the vertex* characterized by headache, nausea, vomiting and convulsions, and, when the meningitis is extremely marked, the signs of the increased intracranial pressure;

(2) *Meningitis of the base of the brain*, leading to involvement of the cranial nerves producing such effects as extraocular muscle palsy, facial paralysis, deafness, and rarely trigeminal neuralgia;

(3) *Involvement of the meninges which surround the optic nerves* producing visual symptoms due to optic neuritis;

(4) *Meningitis of the posterior fossa*, perhaps leading to internal hydrocephalus and the signs and symptoms of increased intracranial pressure;

(5) *Clinical manifestations of spinal cord disease* including root pains, paraplegia, or even tetraplegia, produced by involvement of meninges surrounding the spinal cord;

(6) *Circumscribed gummatous meningitis*, a variety of the late meningeal reaction, very rare, probably more frequently encountered in the region of the spinal cord than within the skull.

The spinal fluid picture in chronic meningitis may be variable. The cell count may be normal or elevated to several hundred lymphocytes. Globulin may be absent or present in large amounts. Total protein may be within normal limits or as high as 100 mg. per cent. The colloidal tests may be normal or range up to the first zone type reaction. The complement-fixation reaction and flocculation tests vary from normal to the most strongly positive. Any combination in the formula of these tests may be found.

Diagnosis depends on an evaluation of the combined clinical and serologic evidence. The prognosis, unless tissue destruction from pressure or scarring has occurred before treatment is instituted, is good. Some cases are satisfactorily managed with the use of standard antisyphilitic treatment, but fever therapy is often required.

**Meningovascular Neurosyphilis.**—There is involvement of the blood vessels as well as the meninges. Probably one type of involvement does not exist without the other; but, when there is clinical evidence of vascular disease, the term meningovascular neurosyphilis is used, implying that the meninges are inflamed. The spirochete invades the blood vessel wall and creates the proper condition for the formation of vascular thrombosis.

Resulting symptoms depend on the location and size of the vessel thrombosed. Loss of consciousness, attacks of dizziness, and mental confusion occur. The symptoms also include monoplegia, hemiplegia, aphasia, hemianopsia, cerebellar syndromes, and all types of psychotic behavior. Thromboses rarely occur in the first 6 to 12 months of the infection. They occur more frequently in the succeeding 5 to 15 years with greatest frequency 5 to 12 years after the infection. Characteristic pupillary signs may or may not be present. The spinal fluid gives a group III formula in about 60 per cent of the cases, whereas in the remaining 40 per cent weaker formulas of any variety are found.

Prognosis in treated cases is not altogether bad. There is often a marked improvement of the signs of paralysis or psychosis in a few weeks. But repeated thromboses may occur. In treatment the combination of fever and chemotherapy is often desirable.

**Tabes Dorsalis (Locomotor Ataxia)** is a type of neurosyphilis in which the posterior roots and posterior columns of the spinal cord show degeneration, with frequent involvement of the midbrain and probably of the sympathetic nervous system. The major symptoms are ataxia, pain, visceral crises, diplopia, disturbance of bladder and sexual function, and loss of visual acuity. These symptoms may occur separately or in combination.

Ataxia, which is due to the diminution of the sense of motion and position sensation, is usually first perceived as difficulty in walking in the dark, trouble in making sudden changes in direction and in walking in a straight line. There is usually a sensation in the soles of the feet described as walking on cotton or on a thick rug.

Pain of an excruciating, lancinating type, often described as if a hot wire were thrust into the flesh or as a pinching of the skin, is characteristic. Such a jab of pain is likely to be instantaneous and repeated over and over again at short intervals for hours or days at a time. Frequently the pain is localized to a small area as in the toe, the heel, the ankle, the calf, the thigh. The pain may jump from one of these areas to another but often remains in the same spot. At first the pains are mild, with long intervals between attacks. As time goes on they become more severe, longer lasting, and more frequently repeated. These pains are often precipitated by cold, wet weather during intercurrent infections, or on fatigue. There are infinite variations of the pat

tern. Some patients describe merely attacks of what seem like a feather being drawn across the skin, mild neuralgic pains, or sensations like an electric current being applied to the skin. Many patients suffer from hypersensitivity of the skin, especially about the trunk, so that the pressure of clothes becomes uncomfortable or getting into a bathtub of warm water is almost intolerable. Some have a sense of constriction about the waist.

*Visceral crises* of the commonest type are related to the upper part of the gastro-intestinal tract, characterized by attacks of nausea and vomiting with or without severe cramplike pains or with pain alone. Rectal crises are characterized by pain in the region of the anus and rectum with tenesmus. Sometimes diarrhea, at other times constipation, is associated. Other crises such as laryngeal spasms occur. Characteristically these crises occur in spells separated by days, weeks, or months. In a typical gastric crisis vomiting may last for days, leading to marked dehydration. There are many variants of the gastric crisis. Occasionally one encounters a patient who has regular morning vomiting. Others speak of periodic attacks of indigestion. Duodenal ulcers are not infrequent in patients with gastric crises.

*Diplopia is a common occurrence in the tabetic, often the first evidence of the disease.* Ptosis of the eyelid is also frequent. Paralysis of accommodation with internal ophthalmoplegia may also occur. Diplopia is the result of partial or complete paralysis of the third, fourth, or sixth cranial nerve, most frequently the third. The symptom often disappears spontaneously in the first attack but without treatment there is likely to be a recurrence, following which a permanent palsy often results.

*Bladder and sexual disturbances* comprise loss of bladder sensation leading to distention, loss of tone, and overflow incontinence and loss of libido and potency—*frequent and sometimes early symptoms.* Patients often boast of their capacity *to hold the urine all day.* After voiding there is usually considerable residual urine. Secondary infection and pyelonephritis are not uncommon.

*Loss of visual acuity due to optic atrophy* is a characteristic sign of tabetic neurosyphilis leading to loss of eyesight and complete blindness. Generally it begins with night blindness and more or less rapidly proceeds to complete loss of vision. At an early stage it may be quite difficult if not impossible to differentiate optic retrobulbar neuritis due to an inflammatory process and true tabetic optic atrophy. When optic atrophy occurs, the other symptoms of tabes are usually minimum.

*The objective signs of tabetic neurosyphilis* include pupillary changes, extra-ocular palsies, diminution or absence of the knee jerks and ankle jerks, disturbance or loss of vibration and position sense of the lower extremities, more marked in the distal portion, Romberg's sign, ataxia, zones of disturbed sensation about the trunk, hypalgesia to pressure on the gonads and the tendo Achillis, hypesthesia across the nose and dorsum of the feet.

*Argyll Robertson pupils*, small irregular pupils which fail to react to light but which react during accommodation, are found more frequently in tabes than in any other form of neurosyphilis. The typical Argyll Robertson pupil is often a relatively late sign and is preceded by irregularity, inequality and poor reaction to light. Although the tabetic pupil is often small, in some instances wide pupils may be found, and sometimes the pupils respond neither to light nor on accommodation.

*Optic atrophy* is demonstrated by the pallor of the optic disk, usually associated by loss of visual acuity, frequently by restriction of the visual fields. The recognition of early optic atrophy by ophthalmoscopy is possible by an expert ophthalmoscopist.

*Tabes dorsalis* is evident, as a rule, only after syphilis has existed for [illegible] years but may develop at any time during the next 25 years. The onset may be insidious, ushered in by flickering pains or by a disturbance in gait or a mild visceral crisis. On the other hand, it may occur suddenly. One occasionally meets a patient who collapses and when helped to his feet is markedly ataxic. The onset of a severe gastric crisis may be the first recognized symptom. In most cases, however, pupillary changes and absence of the tendon reflexes of the lower extremities precede symptoms by many months or years. The course of tabes dorsalis is generally progressive, with an increase of symptoms and signs. However, some cases undergo spontaneous arrest or develop negative spinal fluid, but this is not necessarily paralleled by disappearance of symptoms.

*Spinal fluid findings* of tabes dorsalis vary. In many during the acute stage of advance, one finds a strong formula such as is characteristic of general paresis. Weaker formulas are found even in the early period of progression, and in about [illegible] per cent of the cases there are moderate pleocytosis, a moderate increase in globulin and total protein, a moderately strong colloidal gold and a moderately strong complement-fixation reaction. The spinal fluid may become normal spontaneously.

*Chemotherapy and fever therapy* usually arrest the progress of the inflammatory process, and the spinal fluid may revert to normal. Unfortunately, however, in many of the cases in which symptoms have existed for some months before treatment is instituted, these persist despite the return of the spinal fluid to normal.

*Joint destruction, the Charcot joint, is a complication* resulting from repeated trauma to a joint which has lost some of its normal protective sensitivity to pain. The Charcot joint often occurs in patients who have normal spinal fluids and a history of complete arrest of the other tabetic symptoms.

**General Paresis (General Paralysis of the Insane, Dementia Paralytica, Psychosis With Syphilitic Meningo-Encephalitis)** is a psychosis due to spirochetal invasion of the brain. The pathologic changes, consisting of nerve cell atrophy, perivascular infiltration, gliosis, and chronic meningitis, exist long prior to the development of mental changes which are the sine qua non of the disease entity.

*The mental symptoms of general paresis* duplicate almost any psychiatric symptom complex. The onset of general paresis is usually insidious, although mental symptoms may begin with extreme suddenness. It is usual to obtain a history that, before symptoms were recognized, there was a period of months during which the patient complained of headache, insomnia, capricious appetite, loss of weight, disturbance of sleep, easy fatigability and difficulty in concentration. This galaxy of symptoms is all too frequently *diagnosed as psychoneurosis.* In retrospect, it is generally evident that there was a gradual change in the personality and behavior of the individual, with irritability, mild memory loss, poor judgment, lack of care in personal appearance, defect in moral and ethical conduct, and unexplained deviations in character. In other

patients the psychosis may be ushered in suddenly by a convulsion or a period of confusion. In many patients one obtains a history that, several years before the psychosis was recognized, an epileptiform or apoplectiform seizure has occurred, perhaps accompanied by hemiplegia or aphasia of short duration.

*Classification of several varieties of general paralysis* follows the presenting symptoms of the psychosis

(1) *A simple dementing form* characterized by loss of memory, loss of calculating ability, defects in judgment in association with increasing speech difficulty and tremors;
(2) *The grandiose form* in which ideas of grandeur and a sense of euphoria are paramount;
(3) *The manic form*, in which there is marked similarity to the symptoms of the manic phase of manic-depressive psychosis;
(4) *The depressed form* similar to the depressive form of manic-depressive psychoses;
(5) *The agitated form* duplicating the agitated depressions of the involutional psychoses;
(6) *A schizophrenia-like syndrome* with paranoid, catatonic, and schizophrenic features; and
(7) *Epileptiform manifestation* frequently repeated, often characterized as syphilitic epilepsy.



Fig. 131.—Syphilitic arthropathy. "Charcot joints." (Dr J F [illegible])

*The neurologic signs* encountered in general paresis are invariable. *Pupillary changes* occur frequently but are often absent in the early stage of the disease. Irregularity and inequality of the pupils are the most frequent of these signs found early. Disturbance in the light reaction may occur with the Argyll Robertson pupil or complete fixation ultimately developing. Dilated pupils are more frequent than miosis. *Speech defect* or disorders of articulation are probably the most characteristic somatic disturbance of general paresis. A break in the voice, tremulousness, overactivity of the facial muscles, even including the orbicularis oculi, with stumbling over consonants, should raise the question of general paresis. In the early stages, the speech defect is demonstrated by having the patient repeat difficult test-phrases such as "Methodist Episcopal" or "Third Riding Artillery Brigade," but it is often recognizable in spontaneous speech. *Tremor* is a frequent and early sign and is seen in the facial muscles, the protruded tongue, and the extended fingers. Rapid alternating movements of the hands and fingers are poorly performed. The tendon reflexes are often exaggerated. If tabes is coexistent, they are diminished or absent. Persistent signs of focal damage, when they occur, suggest that the case is not one of pure paresis.

*The course of untreated paresis* is downhill, leading to extreme mental and physical deterioration and death. In untreated cases about one-half die within 30 months of the onset of mental symptoms and almost all are dead within 5 years. During the course of this downhill trend, epileptiform and apoplectiform seizures are frequent. An interesting characteristic of the paretic apoplectiform seizure is the tendency for quick recovery from the apparent focal brain damage. Following each convulsive attack, however, mental deterioration may ensue. From 10 to 20 per cent of patients have spontaneous remissions, lasting for several months to a year, followed by relapse.

*The spinal fluid in general paresis* is characteristic. The cell count varies from normal to 50 or more per c mm; globulin is present in large amounts; the total protein varies from 75 to 150 mg. per cent; the colloidal gold test is of the first zone or

paretic variety The complement-fixation and flocculation tests are strongly positive. Little variation from this formula is consistent with the diagnosis of general paresis.

*The prognosis f general paresis under treatment* is in the majority of cases an arrest, with some residual defect, the extent depending upon the amount of damage which occurred before treatment became effective. Every case in which the physical state of the patient permits should have fever therapy as well as chemotherapy

**Vascular Neurosyphilis**, pure and without concomitant meningeal involvement, is a questionable entity There has been much discussion concerning the diagnosis of vascular neurosyphilis in syphilitic patients who have cerebral vascular accidents and a normal spinal fluid. These are probably usually instances of degenerative arteriosclerosis or hypertension in syphilitic individuals and not primary neurosyphilis.

**Congenital Neurosyphilis (Juvenile Neurosyphilis)** is the term given to neurosyphilis occurring in patients with congenital syphilis. The symptoms may be similar to those seen in adult form of neurosyphilis and usually appear during childhood or adolescence. The most common is that of juvenile paresis. Juvenile tabes and other forms are great rarities.

**Treatment of Neurosyphilis.**—Meningeal syphilis responds relatively quickly and satisfactorily to chemotherapy meningovascular syphilis responds less well; and parenchymatous neurosyphilis, tabes, and general paresis respond little or not at all.



Fig. 332.



Fig. 333

Fig. 332.—Paresis, with hypomania and delusions of grandeur
Fig. 333.—Paresis, with dementia and deterioration.

Penicillin, still being assessed, has considerably altered the programs described hereinafter (see under syphilis, treatment) Penicillin may continuously accompany fever therapy malarial o artificial in doses of 40,000 to 100,000 each 3 hours. A course of therapy we consider probably adequate in any variety f neurosyphilis requires 3 weeks of hospitalization, with artificial fever therapy holding the rectal temperature of 105 F for 4 hours on alternate days 3 times a week to a total f 9 bouts, and penicillin 100,000 units each 3 hours d ring the 3 periods of 5 days during which fever is being given, to a total dose f 12,000,000 units. A course of 10 to 20 injections of 0.2 gm. bismuth at weekly intervals may follow this. We are confident that a patient who completes such a schedule is not undertreated and we have not experienced trouble with t administration. Three artificial feve treatments a week are tolerated by patient who are tolerable of fever treatment at all. During such a hospitalization, we concurrently eliminate focal infection. Penicillin alone improved every type of neurosyphilis followed for from 90 days to 3 years by Stokes et al (AmJS 32 23, 1948) whose results were interpreted to indicate the value of high dosage and repetitions of courses, although subsequent courses of treatment yielded

no great additional effects. Most patients showed most improvement in the first 200 days, and there was little tendency to relapse. Blood tests often failed to improve while the spinal fluid did. Symptomatic improvement was as good after 3 years with penicillin alone as with malaria, but malaria appeared to do more for tabes dorsalis. Penicillin alone is best in asymptomatic neurosyphilis. Dattner (NYSJM 47: 147 1947) compared patients treated with malaria plus chemotherapy and those with penicillin alone: about 65 per cent of both groups obtained satisfactory results. Relapses were highest among those who received less than 5,000 000 units of penicillin. Dattner (AmJS 32 399 1948) reported that only 11 per cent of 301 patients treated with penicillin alone required retreatment, and over half of the original failures responded well to retreatment with larger doses, of which the maximum was 9,000,000 units.

Mapharsen or another oxophenarsine hydrochloride has become the trivalent arsenical of choice. These have the advantage of low toxicity and rapid spirochetocidal activity. Because of their rapid rate of excretion, the optimum interval of administration is at least twice a week. Mapharsen may safely be given as often as every other day for 10 to 30 doses in cases with active disease and without recent arsenical treatment. Administration in this manner is especially useful in syphilitic meningitis. Mapharsen cannot be given during the course of malaria but can be used advantageously during the course of artificially induced fever therapy.

*Fever therapy* with malaria the most prevalently used form, and, all things considered, giving highly satisfactory results, is effective in all forms of neurosyphilis. It is necessary to supplement malaria with chemotherapy for malaria does not satisfactorily protect the patient against late visceral disease.

*Benign tertian malaria* (*Plasmodium vivax*) is most generally used, but for persons immune to it, quartan malaria will usually take among Negroes, Orientals, and people who live in malarious districts. Caution is advisable, and it is better to terminate malaria unnecessarily in a number of cases than it is to lose one patient unnecessarily. Headache, malaise, and anorexia with nausea and vomiting are common features of induced malaria. Lightning pains of tabes and psychotic symptoms of paresis are frequently exaggerated during the fever but generally can be controlled by analgesics and sedatives. Exhaustion and prostration which result from loss of chlorides through sweating can be avoided by the routine administration of 1 to 6 gm. sodium chlorid daily. Malaria causes a rapidly progressive anemia. Hemoglobin determination should be performed at intervals, but interruption of the fever need not be considered unless the hemoglobin falls below approximately 7.0 gm. per cent or the red blood cells below 2.0 million. In approximately one-half of malaria cases, mild jaundice occurs, perhaps from rapid destruction of red blood cells. Rarely deep jaundice develops, usually in association with a large, tender liver; when it occurs, it should be viewed with alarm. The spleen is enlarged in the majority of cases and is frequently painful. Rupture of the spleen followed by death is a remote possibility but occurs in somewhat less than one in a thousand cases. A moderate increase in N.P.N with albuminuria is frequent and of no special importance. However renal failure needs always to be considered and especially watched for in elderly patients. Retention of urine is common in tabetic and taboparetic patients and may require catheterization. The blood pressure falls in every case. A reliable sign of the state of the vascular system is the pulse rate, which normally rises to 120-140 during the paroxysms but should fall promptly to 70-90 with defervescence. A persistently elevated pulse rate, 140-160 during fever 110-120 during afebrile periods, is to be considered a serious sign and calls for termination of the malaria. The diet may be as desired, and every effort should be made to keep the fluid intake at a level of from 3,000 to 4,000 c.c. per day.

Authorities differ on the amount of fever which constitutes an adequate course of malaria. Some carefully calculate the number of hours of fever above 103° F and try to obtain a minimum of 150 hours. Others base the calculations on the number of paroxysms of fever reaching 103° F and above, and try to obtain a total of from eight to twelve paroxysms. Either method is satisfactory.

*Quartan malaria* is less satisfactory than tertian because of the long incubation period of about 3 weeks, the length of time required to obtain an adequate course with paroxysms every third or fourth day and the poor quality of fever which generally occurs. The results of treatment by quartan malaria are, however, good, and the time factor should not deter its use when needed. In individuals found immune to tertian malaria, quartan is the treatment of choice.

*The contraindications for malaria* are age of 60 years or more, unless exceedingly well preserved; cardiac disease with history of congestive failure; hypertension with evidence of renal involvement; extensive renal disease; active or extensive healed pulmonary tuberculosis; thrombophlebitis; cellulitis and other potentially severe suppurative infections and physical debility and malnutrition. Malaria carries with it more than ordinary risk in patients with heart disease with aortic regurgitation, convulsions, severe or uncontrolled diabetes, cirrhosis and other diseases of the liver, severe psychotic condition requiring sedation and tabetic bladder with urinary retention.

*Malaria should be interrupted for* persistent tachycardia (120-140) in afebrile periods; intractable nausea and vomiting; rise in N.P.N. to 70 to 80 mg. per 100 c.c.; severe prostration and debility; severe jaundice; vascular collapse with systolic blood pressure below 70 mm. Hg, cyanosis, weak, thready pulse, and clouded consciousness; convulsions not controlled by medication; severe anemia (below 7 gm. per cent hemoglobin or below 2 million red blood cells); and detection of infection with falciparum parasites.

*Artificial induction of fever* can be accomplished in several ways. There remains some difference of opinion in regard to the relative worth of artificial fever and malaria, but no doubt exists that in experienced hands artificial fever is comparatively safe and effective in the treatment of neurosyphilis. It has the advantage of being con-

trolled as to elevation and duration. The general physical condition of the patient is improved almost at once. The equipment is expensive, and specially trained nurses and doctors are required for constant attendance during, and for several hours after stopping, the treatment. The dangers are burns, heat prostration or heat shock, and death from cardiac or respiratory failure. Adequately trained, cautious workers are able to recognize signals of danger and are prepared to meet them. It is customary with each treatment to prolong the fever at a level of about 105.6° F. for 2½ to 3 hours. *A temperature of 104.1° F. should never be exceeded.* Best results have been obtained by a total of 10 to 15 treatments given twice a week. This type of fever cannot be used in all persons. Some patients, although cooperative, unafraid, and anxious to receive treatment, are unable to withstand the heat. As the rectal temperature rises they become increasingly restless, agitated, mentally confused, and uncontrollable by safe amounts of sedation.

*Typhoid vaccine intravenously* in graduated doses may be used for the production of therapeutic fever. The most practical and the safest method is the dilution of stock vaccine in small amounts of normal saline so that 1 c.c. of solution is equivalent to about 100 million bacilli. For the first treatment a dose of 50 to 75 million is used, for the second treatment 100 to 150 million, and with each subsequent treatment an increment of 100 to 200 million organisms. The temperature response is facilitated by the application of hot water bottles and blankets. If a second injection, one-third to one-half the dose of the first, is given as the fever rises following the original chill, the height and duration of the fever are increased. The injections must be intravenous.

*In patients who have had typhoid fever or recent immunization against typhoid* this method is frequently unsatisfactory but, in the majority, good fevers may be obtained. Frequently after the first and second treatments, many patients have a prolonged temperature rise associated with considerable general malaise, muscle pains, anorexia, and vomiting. Subsequent treatments, however, are better tolerated.

A course of fever by typhoid vaccine consists of 16 to 20 paroxysms with rectal temperatures above 104° F. Results of this type of fever therapy are inferior to malaria and artificial fever.

*Good results are obtained by artificial fever* in all forms of neurosyphilis, but the most satisfactory results are obtained in late meningovascular syphilis and tabes dorsalis. Artificial fever has the advantage over malaria of causing less debility during treatment. In patients with general paresis, the relapse rate is higher among those treated with artificial fever than among those treated with malaria.

*Combined artificial fever and chemotherapy* produce better results, it appears from some studies, than if either is given separately. Various methods are under experimental study.

**Treatment of Special Forms of Neurosyphilis.**—(1) *Early asymptomatic neurosyphilis* (less than two years duration of infection) with minimal to moderate (groups I and II) spinal fluid changes: In general such cases will be detected only after chemotherapy whether given by the standard 6-month system, by more intensive methods of arsenical chemotherapy or by penicillin, since in early syphilis, generally diagnostic lumbar puncture is not performed until the completion of such treatment. These cases may continue treatment on an ambulatory basis. Arsenical and bismuth chemotherapy should be repeated for an additional trial period, using the standard 6 month system, or Mapharsen 0.06 gm. may be given 3 times weekly rather than twice weekly 30 injections to the course, 60 injections in all. At the end of this period of chemotherapy the spinal fluid should be promptly re-examined. If the spinal fluid has not shown improvement toward or to complete normality fever therapy must be given.

(2) *Early asymptomatic neurosyphilis with maximal (group III) spinal fluid changes.* These should at once be given fever therapy.

(3) *Late (more than two years duration of infection) asymptomatic neurosyphilis with group I spinal fluid changes.* Whether detected before any or after previous chemotherapy these may be given standard chemotherapy for 6 months. If there is *no improvement in the spinal fluid, fever therapy is indicated.*

(4) *Late asymptomatic neurosyphilis with groups II or III spinal fluid changes.* Regardless of when discovered these should receive fever therapy at once.

(5) *Asymptomatic neurosyphilis, duration of infection unknown, with groups I and II fluid.* These may be given chemotherapy for 6 months, and if not then improved must be given fever therapy.

(6) *Asymptomatic neurosyphilis duration of infection unknown, with group III spinal fluid changes.* These should be given fever therapy.

(7) *Acute syphilitic meningitis.* These should be treated with chemotherapy for 6 months, and it is essential rather than optional that Mapharsen should be given 3 times weekly to a total of 60 injections in 6 months (2 courses of 30 injections each). Symptoms will disappear immediately in the majority of cases, and the spinal fluid cell count and protein content will be reduced to normal, with varying degrees of improvement in other spinal fluid tests. At the end of this 6 months course treatment may be discontinued if the patient is symptom free and the spinal fluid entirely normal.

*If the spinal fluid Wassermann and colloidal curve,* though improved over the original examination, still show some evidence of positivity although the patient may

be symptom free and the spinal fluid cell count and protein content are normal then a second period of 6 months of similar chemotherapy should be given.

Fever therapy should be given at the end of the first 6 months of chemotherapy if symptoms persist or if the spinal fluid is still strongly positive, relatively unimproved. Fever therapy should be given after the second 6 months of chemotherapy if any abnormality persists in the spinal fluid.

(8) *Diffuse meningovascular and vascular neurosyphilis* These cases should be handled in the same manner as acute syphilitic meningitis except that in certain older patients with focal vascular accidents, especially if complicated by cardiovascular syphilis, the intensity of Mapharsen therapy should be reduced. The utmost diagnostic care must be exercised in these cases t[illegible] exclude general paresis.

(9) *All other forms of neurosyphilis, general paresis, tabes dorsalis, and all cases of primary optic atrophy:* These require immediate fever therapy

*Chemotherapy following fever therapy* may comprise Mapharsen, 0.06 gm., daily for 10 doses, to a total of 600 mg. Subsequent chemotherapy need not be employed unless necessitated by clinical progression or relapse or by the recurrence of spinal fluid abnormalities, especially pleocytosis and increased protein content.

**Results to Be Expected From Treatment.**—I[illegible] *symptomatic neurosyphilis early or lat[illegible]* excellent improvement is expected in terms of prevention of development of clinical forms of neurosyphilis. Especially in patients with group III fluids, some degree of positivity of the complement-fixation reaction may persist for many years even after fever therapy. Other spinal fluid abnormalities should disappear.

*I[illegible] acut[illegible] syphilitic meningitis* results are [illegible]ually clinically excellent, though some cranial nerv[illegible] lesions such [illegible] extraocul[illegible] muscle palsies and deafness may persist. I[illegible] [illegible]dequately treated cases, the spinal fluid usually becomes normal, though in some with group III fluids changes may persist in the complement-fixation test.

*In diffuse meningovascular and vascular neurosyphilis* results are variable, depending on the type of lesion. In general most patients do surprisingly well, both from clinical [illegible]nd laboratory standpoints. The spinal fluid, after showing moderate improvement, may remain positiv[illegible] f[illegible] a long time. Rising cell count and protein content [illegible]re forerunners of relapse. I[illegible] assessing the remission of clinical symptoms in diffuse meningovascula[illegible] neurosyphilis, th[illegible] physician must keep in [illegible]ind neurological residuals which [illegible]re prone t[illegible] result from vascula[illegible] occlusions, cortical scar formations, etc. The development of epileptic seizures or the persistence of painful paresthesias does not necessarily indicate advancement or persistence of the inflammatory process.

*General paresis* from the standpoint of its serious potentialities, both in regard to life expectancy and to residual permanent nerve tissue damage, constitutes a medical emergency. Years of experience have clearly demonstrated that fever is the form therapy which can be relied on to arrest the progress of general paresis in the largest percentage of cases. The ultimate success of therapy is directly related to the duration of symptoms prio[illegible] to the institution of adequate treatment. The disease appears to be [illegible]rrested, with return to excellent functional condition, in about one-third of patients treated. Varying degrees of incomplet[illegible] remission with some degree of residual defect take place in about 60 per cent. I[illegible] [illegible]bout 10 per cent, [illegible]ll forms of treatment are una[illegible]ailing [illegible]nd death is inevitable. Following the termination [illegible]f fever therapy clini[illegible]al improvement usually occurs reaching its maximum [illegible]t [illegible]bout 6 months. Some cases respond promptly. In a few, clinical improvement may be delayed [illegible] year or more. Improvement in spinal fluid cell count and reduction in protein content usually occur within [illegible] few months. Other abnormalities, especially a positiv[illegible] complement-fixation test, may persist for many years. In spite of [illegible]aintenance of a satisfactory clinical status, or [illegible]t least without evidence of [illegible]dvance of the disease process the spinal fluid should be examined regularly at 6-month intervals. The cell count and total protein are the first tests to reach normal levels and are the most sensitiv[illegible] indicators of activity. Persistent elevation or the return to abnormal levels, of either or both of these tests usually precedes th[illegible] development of [illegible] clinical relapse [illegible]nd indicates the desirability of a second course of fever treatment. The spinal fluid complement-fixation reaction [illegible]nd colloidal gold test are less sensiti[illegible]. The[illegible] remaining [illegible]bnormal does not necessarily indicate impending relapse. A complement-fixation test which remains strongly positiv[illegible] or re[illegible]erts to positiv[illegible] [illegible] [illegible] f[illegible] [illegible] 18 months to 2 years after treatment is to be considered [illegible] indication of persistent activity regardless of the other tests, and may foreshadow [illegible] ultimate relapse. A second course of fever may be given t[illegible] a patient with such [illegible] fluid examination.

*I[illegible] tabes dorsalis* in which symptoms develop within the first 10 years of the disease or in which symptoms come on acutely are found the strongest spinal fluid reactions. Paradoxically these are often the cases which obtain the greatest benefit from treatment. Conversely patient[illegible] with a long history of [illegible] visceral crises, lightning pains, and slowly developing [illegible]taxia show the least active spinal fluids and obtain disappointingly little benefit from [illegible] therapeutic treatment.

*I[illegible] optic [illegible]trophy* the results of fever therapy depend on the degree of damage before treatment is instituted. In general, in patients in whom visual acuity in the better e[illegible] is 20/40 or better there is about [illegible] even chance of [illegible]rrest of the [illegible] trophic process and the maintenance of useful [illegible]sion.

**Reviews of Treatment** re f[illegible] neurosyphilis in general, O'Leary (J [illegible] 109 [illegible] 1102, 1937); for tabes dorsalis O'Leary et al. (ADR, 38: 602 1938); for [illegible] rises [illegible]Moore (AmJR 23 782, 1939); [illegible]nd for optic atrophy Moore et al. (J [illegible] 1938; AmJB 4: 89 1940; ib. 26 407 1942) and Bruetsch (J 120 14 19[illegible] texts should be consulted, notably those of Stokes [illegible]f Moore and of [illegible]

## CONGENITAL (PRENATAL) SYPHILIS

**During Pregnancy.**—Prenatal syphilis is a good name for diaplacental infection of the fetus. Infection occurs in utero. In this stage it is usually curable.

Spirochetes have never been demonstrated in fetal tissues earlier than the fourth month and rarely before the fifth. At term, however, the tissues are teeming with them, particularly the liver. The fetus can acquire syphilis from its mother shortly before or at the time of birth. It is generally true, as Kassowitz's law asserts, that there is progressively less likelihood that the successive children of a syphilitic mother may be infected, for with the passage of time the woman's immunity is likely to prevail; yet it happens that the disease may skip one pregnancy to damage the next, a phenomenon explicable on the assumption of variations in the degree of immunity of the mother.

Showers of spirochetes occur from time to time in any syphilitic person, it is thought. If this happens in a pregnant woman, the fetus will be infected. Since it may happen, it must be prevented from happening. The Cooperative Clinical Group (J 106: 464, 1936) concluded: "The data show that congenital syphilis is practically a preventable disease. *Its prevention is dependent on the routine, early and repeated use of the serologic blood test on every pregnant woman and on adequate treatment once the diagnosis of syphilis has been made.*"

Treatment should be begun before the fifth month of pregnancy. It should be adequate, and, before penicillin, comprised preferably 10 or more *injections of* arsphenamine and also an appropriate heavy metal. If early syphilis appears late in pregnancy proper treatment carried through term will increase the likelihood of the birth of a healthy baby. To insure a living nonsyphilitic infant, it is necessary to treat the mother during each pregnancy, thought Peckham (J 117: 1563, 1941). *It is* not necessary for a woman who has had syphilis to undergo treatment during every pregnancy provided that she has received 4.0 gm. of Mapharsen or its equivalent or 2,400,000 units of penicillin, and provided that she is without signs of active syphilis and has negative STS or STS of 8 units or lower titer, wrote Goodman and Farber (AmJS 32: 409, 1948).

Some 25 per cent of the pregnancies in syphilitic families result in miscarriage or stillbirths, and fetal death is at least twice as frequent in syphilitic as in nonsyphilitic families. The earlier in pregnancy that antisyphilitic treatment is given, the greater the probability of its success in securing a nonsyphilitic offspring (Solomon: J 129: 500, 1945).

Massive arsenical therapy is ill tolerated by the pregnant woman, who is more liable than other syphilitic patients to the hazards of hemorrhagic encephalitis (Speiser et al.: AmJOG 49: 14, 1945); *it should never be used.* The reaction rate to arsenicals increases as the pregnancy progresses (Kennedy and Hennington: ADS 43: 83, 1943). *Penicillin is especially effective in the treatment of syphilitic pregnant women* (p. [illegible]) and is safe. It is, in fact, so superior for this purpose, protecting the child even when started late in pregnancy, that it supersedes all other possible choices (Aron et al.: ADS 56: 849, 1947).

*Immunity in the infantile type of disease is as variable as in the adult.* Miscarriage, stillbirth, prematurity and actively syphilitic living babies are the results of severe infection, yet normal babies may be born to syphilitic women. Babies with syphilis may for many years show no symptoms of activity of the disease. Infection in the fetus damages structures while they undergo embryologic development.

Colles (183 ) noted that an apparently healthy man might marry and transfer syphilis to his wife without showing any evidence of the disease himself. Colles' law states that a woman without obvious venereal symptoms may bear a syphilitic child and nurse it with impunity even though others are infected by it. Profeta (1865) saw apparently healthy children being nursed by obviously syphilitic mothers without becoming infected. It is generally believed at present that if the child is diseased the mother must be infected although her disease may be latent.

**Third Generation Syphilis**, the transmission of infection from a congenital syphilitic to his offspring, possibly occurs, although the difficulty of proving this is evident (Brussel: ADS 40: 70, 1939).

**In Twins**, congenital syphilis occasionally affects the one and not the other (Smith and Spence: HMJ 34: 147, 1941).

**Acquired Syphilis in Infancy and Childhood** has frequently been observed (Creswell et al.: AmJDisChild 66: 611, 1943). A newborn with a scalp chancre pre-

sumably inoculated in the birth canal, was noted by Quiroga (abs. ADS 42 661, 1940). Sad circumstances of transmission by nonsexual contact were reported by Murrell and Gray (BMJ 1:206, 1947)

**Early Symptoms.**—Cutaneous lesions may be present at birth, or may develop during the first 4 or 5 months. Syphilitic babies are generally marantic, emaciated and feeble, with thin, wrinkled skins, and wizened, senile faces. Coryzal symptoms, often accompanied by rhinitis, snuffles, and hoarse breathing may be among the earliest manifestations. Mucous patches and condylomas are likely to be present during the first few months, and these lesions often develop prior to the appearance of the general exanthem. The character of the cutaneous eruption varies. Bullous lesions may occur in hereditary syphilis. The blebs range in diameter from 1 to 5 cm., and are usually only partially distended, with eroded bases, and flabby fragile walls. Such lesions may be generally distributed, but often they are limited to the palms and soles. They are likely to be intermixed with macules, maculopapules, and occasionally pustules. Lymph node involvement is often present, but is not a typical or characteristic feature. The commonest types of eruption are the papular and maculopapular. Fissures of the lips, angles of the mouth, and anus are present in some three-fourths of the cases. Pustular lesions, like bullae, usually indicate a grave infection. Tubercular and gummatous lesions seldom occur early in the disease. See Cole et al. (VDI Suppl. 7 1940) Wile and Hundt (AmJS 26 70 1942)

The early manifestations of prenatal syphilis (Cole J 109 580 1937) correspond to the secondary stage of acquired syphilis. Ordinarily they show up some weeks after birth. Prenatal syphilis can ape any of the characteristics of acquired syphilis, excluding cardiovascular manifestations. The child is restless, cries feebly but frequently and has snuffles. A reddish brown or coppery eruption is seen most frequently on the palms, soles, and diaper area. It is comparatively easy to find *S. pallida* by dark field examination of material from the paronychium, the rhagades, and moist papules or bullae. General examination reveals an enlarged liver perhaps down to the level of the umbilicus, and an enlarged spleen.

Disease of the bones is found in a fair percentage of the cases, consisting of thickening at the end of the long bones, especially the radius and ulna. Owing to pain the child holds the limb as if it were paralyzed (Parrot's pseudoparalysis). X ray examination reveals the characteristic epiphysitis (Black JPed 14 761, 1939) from which must be differentiated the lines caused by bismuth therapy given to the mother (Whitridge AmJS 24 223 1940). Periostitis and occasionally dactylitis are seen. Roentgen findings thought most trustworthy in diagnosis by Black are (1) well-defined saw tooth metaphysis in well-calcified bones (2) multiple separation of epiphyses, with or without impaction, in bones which are not rachitic (3) bilaterally symmetric osteomyelitis of the proximal medial aspects of the tibiae (4) multiple circumscribed osteomyelitis of long bones showing patchy areas of rarefaction (5) multiple longitudinal areas of osteomyelitic rarefaction in the shafts of long bones, sometimes resulting in fractures (6) foci of destructive rarefaction at the medial or lateral aspects of the metaphyses and (7) multiple areas of cortical destruction generally seen within 1 cm. of the ends of the bones. More osseous lesions are to be found in infants less than 5 months old and are of the form of generalized osteochondritis and periostitis after 1 year osteitis and os--



Fig. 334.



Fig. 335.

Fig. 334.—Fissures of labial commissures and snuffles. (Dr Sam Sweitzer.)
Fig. 335.—Prenatal syphilis marasmus, snuffles, labial fissures (Dr H. N. Cole.)



Fig. 336



Fig. 337

Fig. 336.—Prenatal syphilis. Active syphilitic dermatitis, bullous syphilid of palms and soles. (Cole J 109 580, 1937.)
Fig. 337.—Popliteal gumma in a congenital syphilitic, 10 years old.



Fig. 338.

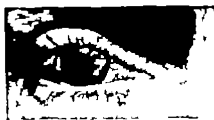


Fig. 339.

Fig. 338.—Rhagades, scars of prenatal syphilis of face. (Dr F Ronchese.)
Fig. 339.—Interstitial keratitis of right eye. (Dr C. O. Dennie.)



Fig. 340.

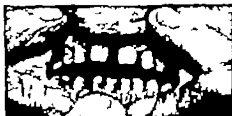


Fig. 341.



Fig. 342.

Fig. 340.—Saddle nose (Dr J P Gosquierra.)
Fig. 341.—Syphilitic dental stigma: notching, wide spacing, narrowing of occlusal margins. (Dr Grover Wende.)
Fig. 342.—Syphilitic periostitis.



Fig. 343.—Osteitis in prenatal syphilis; defects of ends of radius and ulna. [illegible]

myelitis are usual and periostitis is seen (Russo and Shryock Radiol 44 477 1945) See Hill et al. (JPed 30 547 1947)

**Late Symptoms.**—There is a late stage of prenatal syphilis, as of acquired syphilis, in which the disease has a tendency to localize itself to certain parts or organs (Smith AmJS 24 755 1940) In the Cooperative Group study approximately 33 per cent suffered from parenchymatous or interstitial keratitis, 12 per cent had involvement of the central nervous system, and 7.2 per cent had involvement of bones and joints.

Gummas may affect the bony structure anywhere but are found most frequently in the tibia, skull, bones of the nasopharynx, and bones of the upper extremities, especially the inner end of the clavicle. Trauma is a factor in their localization. Saddle nose results from destruction of the bones of the nose. Gummas may affect soft parts as well as bony structures. Late involvement of the bones occurs most frequently in the form of diffuse osteitis or in a form of chronic hydrarthrosis of the joints (Clutton's joints) The knees are most frequently affected (Loos AfDuS 181 549 1940) Osteoperiostitis is a diffuse hyperplastic process most often affecting the tibia. The periosteum is inflamed, and there is thickening from new bone formation leading to the saber shin appearance. The enlargement of one sternoclavicular articulation Higoumenakis sign, is as significant of the existence of late prenatal syphilis as are other important stigmas (Yang ADS 41 1060 1940)

The teeth often show deformity (Karnosh ADS 13 5 1926) The true Hutchinsonian incisor shows deformity of the developmental lobes of the permanent central incisor and is not due to transitory calcium deficiency The true mulberry molar of syphilis is a permanent first molar characterized by enamel cusps showing crests of sound enamel on a base of hypoplastic deposits. The cusps are generally crowded together on a crown surface of dwarfed dimensions. The upper incisors especially are narrowed and somewhat smaller than normal, are bowed out on their sides, and show a central depression of the cutting edge due to hypoplasia of the middle lobe Dwarfing of the affected tooth and lack of development of the premaxilla were the abnormalities stressed by Johnston et al. (Am J Orthodont. 27 667 1941) who could not demonstrate spirochetes in the dental structures. The effects of syphilis on the teeth depend upon the developmental stage during which the disease was active, and roentgenologic diagnosis from studies of unerupted permanent teeth can often be made, according to Sarnat et al (J 116 2745 1941) The teeth especially affected are the permanent upper central incisors, the lower central and lateral incisors and the first molars (Sarnat and Shaw AmJDisChild 64: 771, 1942) Dental anomalies occur in approximately half of all heredosyphilitic children.

The central nervous system is commonly involved. This seems more frequent in the earlier years of life than later An incidence of from 20 to 40 per cent has been quoted Syphilitic meningitis gives evidence of pressure symptoms the fontanel is tense, acute hydrocephalus may be present, and convulsions may occur The spinal fluid shows the usual changes. Paralyses of various types are also seen in these young patients With parenchymatous involvement of the brain tissue, juvenile dementia paralytica is encountered The symptoms may show up at any time from the age of 5 or 6 years to 20 or 25 In cases in which there is involvement

of the posterior columns of the cord, the picture of tabes dorsalis presents itself, often accompanied by optic atrophy

Deafness is a distressing result of late prenatal syphilis. It may be mild or total. It may come on slowly or at a certain stage progress with great rapidity. If it has progressed far, it does not respond well to therapy. It usually reveals itself from the age of 6 or 8 years to the age of 20 or 25. Hutchinson's syndrome is not always evident: in 25 per cent all 3 symptoms, deformities of the eyes, ears, and teeth are noted. Changes in the internal ear and deformities of the teeth are present in about 10 per cent, involvement of the eyes and ears in 40 per cent, and involvement of the internal ear alone in 25 per cent.

Ocular manifestations of some kind develop in about 5 per cent of all syphilitics at some time during their disease according to Woods (AmJS 27: 133, 1943). From birth until age 2 years, optic neuritis, choroiditis and retinitis are not extraordinary and the results may be either progression and atrophy or recovery. Between the ages of 2 and 8 years, interstitial keratitis is the usual ocular finding. After the age of 8 years occur interstitial keratitis, eighth nerve deafness, neurosyphilis and optic atrophy.

Of 532 patients with interstitial keratitis, 40 per cent had dental stigmata, 35 per cent bone and joint lesions, 10 per cent labyrinthine disease, 8 per cent chorioretinitis, 8 per cent neurosyphilis (Klauder and Vandoren: VDI 22: 307, 1941). When one eye only was involved, the disease became bilateral within 1 month in 42 per cent and within 10 years in 79 per cent of the cases. Interstitial keratitis may appear any time from 4 or 5 years of age to 20 or 25 years. The cornea develops a diffuse ground glass appearance different from the sharply defined phlyctenules seen in tuberculous keratitis. There are extreme photophobia, lacrimation, and circumcorneal injection of the ciliary vessels. These vessels may invade the cornea. In severe cases there may be iritis, changes in the choroid and peculiar opacities in the vitreous. It is common for the second eye to become involved, especially when therapy has been neglected, and blindness is the result. Slit lamp examination of the corneas may reveal interstitial keratitis which is asymptomatic (Klauder and Cowan: J 113: 1624, 1939). The exact mechanism whereby syphilis damages the cornea is not known, although spirochetes are plentiful in all parts of the eye of the congenitally syphilitic fetus (Woods: AmJS 27: 133, 1943).

Cardiovascular involvement in congenital syphilis is rare, occurring in interstitial and nodular forms. Arteritis but not valvulitis may be caused (Hinrichson: AmJS 27: 319, 1943).

**Pathology.**—In the umbilical cord, the inflammatory infiltrate is rich in polymorphonuclear leucocytes, which are not a usual feature of syphilitic tissue reaction. Scrapings from the umbilical cord examined by dark field prove positive in about 50 per cent of the cases. The placenta is larger than usual and has thickened, rather avascular villi. In some cases it reveals little and yet the child shows plenty of positive evidence. Dippel (AmJOG 47: 369, 1944) did not find spirochetes in any fetus younger than 18 weeks in 67 necropsies of syphilitic infants. Spirochetes in large numbers are in the liver, spleen, kidneys, adrenals, heart muscle, bone marrow and testes. Diffuse fibrosis is seen particularly in the lungs, pancreas, heart, and adrenals. The liver may show areas resembling gummas but which are infiltrated with enormous numbers of spirochetes.

The involvement of bones in the fetus may be recognizable, even before birth, by x ray examination

**Diagnosis** is usually easy when the disease is clinically in evidence. Mucous patches and *condylomas* about the mouth and anus are characteristic features. The occurrence of palmar and plantar bullae also is almost pathognomonic. Roentgenograms are diagnostic in a higher proportion of cases than serologic tests (Evans J 115 197, 1940). Quantitative tests showing significant increase in titer of reagin in syphilitic infants after 4 to 8 weeks, aid in diagnosis (Ingraham ADS 43 323 1941)

### LANDMARKS OF TARDIVE HEREDOSYPHILIS (STOKES)

MAJOR (strongly presumptive or diagnostic)

- Positive blood Wassermann.
- Interstitial keratitis.
- Hutchinsonian incisors.
- Mulberry molars.
- Eighth nerve deafness.
- Epiphysitis and osteochondritis.
- Saber tibiae
- Osteitis of the nasal septum.
  - Snuffles.
  - Saddle bridge.
- Early dactylitis.
- Splenomegaly before the fourth month.
- Rhagades and scars.

SECONDARY (alone insufficient for diagnosis)

- Frontal bosses.
- Aplasia of incisor teeth.
- Scaphoid scapula.
- Marked enlargement [illegible] r third of clavicles (old osteitis)
- Disturbances of age development ratio.
- Precocity and irritability
- Early epitrochlear adenopathy
- High narrow palatine arch.

MINOR

- Venous ectasia.
- Hypertrichosis.
- Ulnar deviation of middle fingers.
- Constitutional subnormality
- Backwardness
- Hypertrophic frontal suture.
- Craniotabes
- Bilateral dacryocystitis in childhood.

DEBATABLE

- Carabelli tubercle
- Retromastoid adenitis
- Persistent infantile hydrocele
- Hypertrophic thymus and thymic abscess.
- Alopecia areata in children.
- Knock knee elbow
- Urticaria and asthma in young children
- Absence of the xiphoid process

Practically 100 per cent of persons with prenatal syphilis have positive serologic reactions. Early treatment is likely to reverse these but the longer the child remains positive and untreated the less likely is therapy to influence the blood test. The cord blood test is not a dependable guide as to the existence of syphilis in the newborn because his serum is likely to react as the mother's does, especially his cord blood serum though the infant may be nonsyphilitic. If physical and roentgen examinations of the infant are negative quantitative tests at intervals of 2 weeks are indicated. Persisting high titer or increase of titer for 6 to 8 weeks justify treatment. In the nonsyphilitic infant with positive tests at birth titer is usually as low as 4 to 8 units within 3 weeks, or negative but occasionally positivity persists into the third month. When the test is positive at the age of 8 weeks, there is 90 per cent likelihood of the coexistence of positive x ray changes. It is inadvisable to give antisyphilitic treatment to infants of syphilitic mothers unless the infants are proved to have the infection

**Treatment.**—Antenatal treatment of syphilitic women prevents syphilis in babies. Penicillin is the best therapeutic agent.

General measures include hygienic and supportive efforts. The nose should be kept clean the folds of the skin should be free from moisture and dirt, and such mucous patches or condylomas as may develop should receive topical attention though they respond promptly to specific therapy. Frequent baths, followed by the liberal application of a bland dusting powder, are useful. Hospitalization and expert pediatric care are highly desirable, for many congenitally syphilitic infants suffer severe anemia, dehydration, hypoproteinemia and difficulties of salt and water balance.

Prior to the introduction of penicillin, which has by now become recognized as the drug of choice because of its effectiveness, safety and coincidental value against the intercurrent infections debilitated infants usually suffer (QMN J 131 1538, 1946) it was judged correct to start the child who had active prenatal syphilis on arsenical treatment at once, giving neoarsphenamine, from 0.01 to 0.015 gm per kg. Intravenous dosage requires some skill the fontanel may be punctured to introduce the medicine into the superior sagittal sinus. The drug is dissolved in 2 cc. of distilled water. Moore at one time preferred sulfarsphenamine from 0.010 to 0.015 gm. per kg., administered intramuscularly into the buttock in a concentrated solution. Ordinarily a course of 8 weekly injections of either preparation was employed immediately followed by a series of weekly intramuscular injections into the buttock of a preparation of bismuth, such as the oil suspension of bismuth salicylate, 2 mg per kg. (Naef and Vieth SMJ 33 691, 1940). Courses of the two drugs might be alternated until a year of therapy has been completed, about 25 injections of each preparation (Howard JPed 14 220 1939). If the serologic reaction was still positive at the end of the year further treatment for 6 months or a year was in order. Mapharsen and bismuth were preferred by Astrachan and Cornell (J 121 740 1943).

The use of acetarsone popular because of the simplicity of its oral administration is of debatable wisdom. The antisyphilitic activity of acetarsone was demonstrated by Pillsbury and Perlman (ADS 39 969 1939) who observed its ability to reverse serologic tests, but serious reactions occurred in 4.6 per cent of their 87 cases. Lyon and Miner (JPed 15 13 19 1939) considered it as good as other arsenicals. The dose may follow the schedule of Maxwell and Glaser (AmJDisChild 43 1461 1932) consisting of 14 gm in 49 days, giving one-fourth of the 0.25 gm tablet daily the first week, twice daily the second week, three times daily the third week, four times daily the fourth week three times daily the fifth week, four times daily the sixth week, and twice daily the seventh week. Such a course is repeated 3 times, with 6 week intervals of rest between courses. Nephritis is the serious reaction most to be feared. Acetarsone may be dismissed today as a dangerous drug, superseded by safer and more effective agents for the treatment of congenital syphilis.

Penicillin was reported effective in a total dose of 18,000 units per pound by Lentz et al. (J 126 408 1944) who at that time believed that the first doses should be cautiously small to avoid serious reactions. It is now known that such a total dose is much too small 70,000 units per pound being perhaps adequate that caution in the first injections is not necessary that the anticipated cure rate in young infants with syphilis

approaches 90 per cent, and that no adjunctive chemotherapy is necessary in the early period of treatment. When 70 000 units per pound are given in 60 doses at 3-hour intervals, seronegativity does not promptly appear but the number of patients becoming seronegative increases monthly for at least 18 months (Platou et al. AmJDisChild 72 635 1946) Larger doses continued over a longer period of time result in improvement in results (Ingraham et al. J 130 694, 1946) It may be recommended that 120 doses be given at 3-hour intervals for 15 days, following which the infant should be examined at monthly intervals with titered serologic tests as long as the tests show positivity. Intervals for re-evaluation may be lengthened to 3 months after seronegativity is attained, and the spinal fluid must be examined about 1 year later. If infectious relapsing lesions occur at any time after the commencement of treatment or if the serologic test is still strongly positive after a year of posttreatment observation, retreatment on an individualized basis is to be considered.

The spinal fluid must be examined early and if this shows evidence of involvement of the central nervous system suitable modification and intensification of treatment must be devised.

The dose of penicillin recommended by Platou et al. (J 133 10, 1947) on the basis of studies of 252 cases treated with penicillin in 5 university clinics, was 100 000 units of penicillin sodium per kg. body weight divided into 120 equal injections given at intervals of 3 hours in a period of from 12 to 15 days. Results included dramatic clearing of active manifestations of infection 6 relapses within 11 months, seronegativity in the majority of the patients within 4 to 12 months following therapy and 27 deaths from all causes. Results from a single course were satisfactory in 73 per cent of the cases, unsatisfactory in 9 per cent, and uncertain in 18 per cent. When spinal fluid abnormalities were present at the outset, they *improved remarkably*. See *Platou and Kometani* (Pediat. 1 601 1948)

In children from 6 to 8 years of age are found osteitis, periostitis, interstitial keratitis, and involvement of the central nervous system. Here an oxophenarsine derivative can be administered intravenously and it is wise to use alternating courses of arsenical and bismuth compounds with no rest periods between courses. Penicillin is highly effective (Yampolsky and Heyman J 132 368 1946)

Around puberty interstitial keratitis, eighth nerve deafness, and involvement of the central nervous system are the great problems. Any of these requires the care of an expert. In interstitial keratitis, fever therapy *the routine use of a cycloplegic, and full doses of chemotherapy comprising* at least 20 doses of the arsenical, seem to be of greatest value (Klauder and Vandoren AOphth 26 408, 1941) In 42 per cent of their 532 cases the eyes were involved either simultaneously or within one month of each other. The second eye of 79 per cent was involved by the tenth year. The final visual acuity of both eyes of 64 per cent of the patients treated continuously was good as compared to 47 per cent of patients treated intermittently or irregularly. Routine treatment supplemented with fever therapy either malarial or artificial successfully prevented relapse in all but 1 of 55 patients so treated. Penicillin in a dose of 50 000 units each 4 hours *failed to prevent involvement of the second eye* in approximately half of 72 cases even when fever was used in adjunct (Klauder AmJS 31 575 1947) The addition of penicillin did not improve the results of adequate treatment entailing 20 doses of arsenic and 8 to 10 hours

of fever The child treated for prenatal syphilis early and adequately is not so disposed to develop interstitial keratitis later Fever therapy by means of typhoid antigen and concomitant penicillin proved not highly satisfactory in terms of clinical results, wrote London and Noojin (AmJS 32 483 1948) who expressed the wish that better treatment were known

Eighth nerve damage is extremely resistant to therapy which should comprise that appropriate to central nervous system syphilis, requiring adequate fever and chemotherapy

Juvenile neurosyphilis is estimated and attacked as adult neurosyphilis is, the spinal fluid findings being significant criteria of activity of the disease. Penicillin and fever therapy are effective in the meningovascular varieties, but juvenile paresis and tabes dorsalis have a poor prognosis (Meninger Juvenile Paresis, Williams and Wilkins, 1936 Nielsen et al : ADS 45 688 1942)

# DERMATOSES DUE TO FUNGI

## DERMATOMYCOSES

**Classification.**—There are many kinds of parasites which affect the human being. The mycoses are the diseases caused by fungi. Bacteria, the Schizomycetes, botanically are members of the fungi; they are considered in the preceding section. Schizomycetes are typically unicellular plants; the cells are usually small and relatively primitive in organization. Higher fungi form a large heterogeneous group of plants including all those lacking chlorophyll. In most of them the vegetative body is surrounded by cell walls and usually appears as septate filaments called hyphae. The vegetative hyphae are collectively known as mycelium. Hyphae grow by the sprouting of small protuberances which enlarge, round off and are cut off from the mother cells by septums. Daughter cells, or sprout cells, are known as blastospores. Among the yeasts this is the only type of vegetative body. When growth conditions are unfavorable resting cells are formed, called chlamydospores. When circumstances become favorable the chlamydospores develop normal vegetative mycelium. Hyphae generally are intertwined in silky masses, which generally are capable of absorbing food at any point. Various specialized structures develop from them. Most fungi, at certain ages and under favorable conditions of nutrition, develop reproductive structures on the mycelium. These are usually spores. Spores are cells or groups of cells characteristically formed and able to grow independently into new individuals. In many fungi there is a sexual function involving the two processes: fertilization, comprising the fusion of two nuclei, and meiosis, in which there is a return to the single chromosome number. Some fungi live without such reconstruction of their nuclei and propagate themselves by imperfect stages only. Such fungi with incomplete or with incompletely known life cycles are called *Hyphomycetes*, or *Fungi imperfecti*. (Dodge, C. W.: Medical Mycology, Mosby, 1935.) Fungus dermatoses are due to fungi imperfecti. The ability to thrive on keratin distinguishes the few pathogens from the many non-pathogens, in general.

**Mycotic Diseases** are by no means limited to the skin, but their conspicuous manifestations are most often cutaneous (Gregory: BiolRev 10: 208, 1935). See Lewis and Hopper: *Introduction to Medical Mycology*, ed. 3, Year Book Publishers, 1946.

Bilateral, superficial, circumscribed, erythematous and scaly eruptions of the upper parts of the inner aspect of the thigh are commonly caused by *Epidermophyton rubrum*. One may often correctly suspect that an infection of the scalp is caused by *Microsporum lanosum* from the history of contact with an infected animal, the short duration, the tendency to heal spontaneously and the inflammatory character of the lesion. Infection of the skin due to *Monilia albicans* and the lesion of blastomycosis, actinomycosis and sporotrichosis are usually expressed clinically in fairly characteristic ways. One may often recognize the identity of *Trichophyton purpureum* as the infecting organism from clinical inspection alone (Lewis and Hopper: AMA 35: 481, 1937). However, the diseases produced by closely related organisms may not be distinguishable clinically. It is practical to discuss dermatomycoses according to their sites.

**Dermatomycosis** includes all cutaneous infections due to fungi.
**Dermatophytosis** is applicable to superficial infections.
**Epidermophytosis** implies infection with an *Epidermophyton*.
**Trichophytosis** is similarly limited to parasitism with a *Trichophyton*.

**Human Pathogens Most Commonly Met in the United States** are listed with their identifying features (Lewis and Hopper).

*Direct examination*: this description usually refers to the microscopic appearance of the organism following the mounting of specimen in 10 per cent aqueous solution of potassium hydroxide.

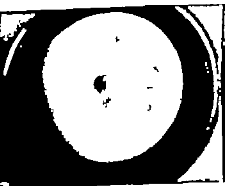


Fig. 344

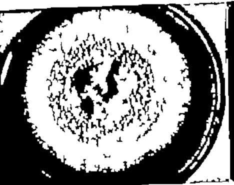


Fig. 345

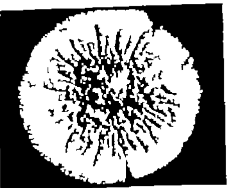


Fig. 346



Fig. 347



Fig. 348



Fig. 349

Figs. 344–349.—Giant colonies of common pathogenic fungi. (Courtesy of Dr. George M. Lewis and Dr. Mary Hopper.) Fig. 344.—*Trichophyton gypseum* (*Trichophyton interdigitale*). Fig. 345.—*Trichophyton gypseum* (granular). Fig. 346.—*Epidermophyton inguinale*. Fig. 347.—*Microsporum lanosum*. Fig. 348.—*Trichophyton purpureum*. Fig. 349.—*Microsporum audouini*.

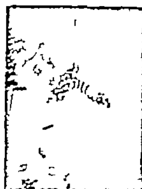


Fig. 330.



Fig. 331.

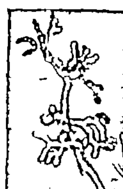


Fig. 332.

Figs. 330-332.—Microscopic characters of common pathogenic fungi. (Courtesy of Dr George Lewis and Dr Mary Hopper.) Fig. 330.—*Trichophyton gypseum*: spirals are characteristic of *T. gypseum*. Fig. 331.—*Trichophyton crateriforme*: microconidia may be attached or unattached singly or in clusters, and are seen in many species of fungi. Fig. 332.—*Achorion schoenleini*: favic chandeliers are characteristic of *A. schoenleini*.

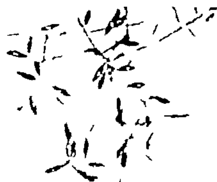


Fig. 333.



Fig. 334.

Figs. 333 and 334.—Microscopic characters of common pathogenic fungi. (Courtesy of Dr George Lewis and Dr Mary Hopper.) Fig. 333.—*Microsporon fulvum*: microconidia, or fuseaux, attached to the hyphae, indicate either *M. fulvum* or *M. lanosum*. Fig. 334.—*Microsporon lanosum*: detached macroconidia, showing septations.

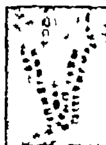


Fig. 335.



Fig. 336.



Fig. 337.

Fig. 335.—*Trichophyton* stained in celium. (Dr B. B. Beeson.)
Fig. 336.—Tinea capitis [illegible] hair. (Dr Stuart Way.)
Fig. 337.—*M. audouini* from tinea capitis. (Dr B. B. Beeson.)

*Cultural characteristics* are as seen after isolation on a solid medium containing 4 per cent crude American dextrose, 1 per cent Fairchild's peptone, and 1.8 per cent agar

*Culture mount* refers to the microscopic appearance of a cultural growth as seen in a hanging drop preparation, in a Henrici slide culture, or in a direct mount from a culture of material in 10 per cent potassium hydroxide solution. The last type of mount is not advisable for routine use because, so prepared, the arrangement of fungus elements cannot be studied satisfactorily

**Microsporum audouini** (commonly causative of tinea capitis).

*Direct Examination.*—Short, broken-off hairs are extracted for examination. The spores are round, small, and grouped to form a mosaic sheath around the infected hairs. There is usually no tendency to the formation of chains.

*Cultural Characteristics.*—The colony is slow growing, consisting of close-matted, velvety aerial mycelium, light gray to brown in the center with radiating furrows. The reverse of the colony is reddish-brown to orange in color

*Culture Mount.*—Fuseaux and microconidia are occasionally seen. Chlamydospores and pectinate bodies are frequent.

**Microsporum canis (M lanosum)** (commonly causative of tinea capitis).

*Direct Examination.*—Hair infected with *M. canis* cannot be distinguished from hair infected with *M audouini*. In scrapings from lesions of tinea circinata, segmented mycelium may be noted.

*Cultural Characteristics.*—The growth appears first as a downy fluff, and it develops fairly rapidly After 2 weeks the colony is woolly and the aerial material is abundant. The color is buff tan. The development of yellow pigment on the undersurface of the colony is characteristic. Grooves may be radial or concentric Pleomorphism begins after 4 or 5 weeks. The appearance under the filtered ultraviolet rays (Wood light) is distinctly lavender blue or shell pink toward the center of the colony the colors being bright and clear

*Culture Mount.*—The feature of this fungus is the presence of large numbers of fuseaux of the tapering sort. Microconidia and some other forms may also be noted.

**Microsporum gypseum (M. fulvum) (Tinea)**

*Direct Examination.*—A hair infected with *M fulvum* may resembl in appearance hair infected with any ther *Microsporum*. Sometimes spores in linear arrangement may be observed.

*Cultural Characteristics*—The growth is flat, felty, and cinnamon brown A central umbo may be present. Concentric furrows sometimes ppear Pleomorphism is usually manifest after several weeks. The reverse of the colony is reddish-brown to orange in color.

*Culture Mount.*—Numerous fuseaux are present Racquet mycelium, nodular organs, and small round spores may also be seen.

**Trichophyton (Achorion) schoenleini (Favus)**

*Direct Examination.*—Large spores in chains are noted in the substance of the hair The presence of air bubbles is almost of diagnostic significance. Sporulated mycelium will be found in large amounts in scutula but are few in number in infected nails or in superficial lesions of the smooth skin.

*Cultural Characteristics.*—After 3 or 4 weeks the growth is smooth, compact, and waxy The surface shows numerous folds. Pleomorphism is rare. The submergence of the colony usually results in cracking of the agar

*Culture Mount.*—Favic chandeliers may be noted. Chlamydospores in large numbers may also be observed.

**Trichophyton sulfureum.**

*Cultural Characteristics.*—At first, the colony is elvety with a central red nodule, the rest of the culture showing a delicat primrose color. Later it becomes powdery folded with a small central crater and becomes sulfur yellow in color

**Trichophyton mentagrophytes (gypseum) (Tinea).**

*Direct Examination.*—In a follicular infection, small, round spores in chains may be found external to the hair. In scales macerated tissue, or in nail scrapings, chains of spores or segmented mycelium with little branching will be noted.

*Cultural Characteristics.*—There re 4 types of growth which Lewis and Hopper believe are closely related genetically

1. The usual type. This begins as a white, fluffy growth. After bout 2 weeks, the surface becomes velvety and buff-colored. There is usually a boss at the center and a few irregular folds.
2. The granular variety The surface is powdery and is light buff or maize yellow in color Fluffy changes develop with age.
3. The T interdigit le type. This begins as a downy projection, developing int white, fluffy, diffuse growth covering an agar sla t within 2 weeks.
4. The T niveum type. This is white and fluffy at first, later becoming compact. Surface irregularities are present.

*Culture Mount.*—

1. The usual type. Spirals may be seen. Small numbers of fuseaux, nodular organs, pectinate bodies, racquet mycelium, and chlamydospores may be noted. Microconidia are present.
2. The granular type. Numerous fuseaux are present and dense masses of microconidia are to be seen. Few spirals will be seen. Chlamydospores and racquet mycelium may be found in the subsurface growth.

3. The *T. interdigitale* and *T. niveum* types. A large number of filaments and few clusters of microconidia are observed. Nodular organs and racquet mycelium may be found. Spirals and fuseaux are usually absent.

**Trichophyton rubrum (purpureum) (Tinea)**

*Direct Examination.*—There is nothing characteristic in the microscopic appearance of the fungus in scrapings. While the amount of fungus material may be sparse, large numbers of organisms have been noted in an occasional specimen. The mycelium is about the same size as that of *T. gypseum*, being 3 or 4 microns in diameter.

*Cultures.*—On dextrose agar primary growth at first is fluffy, pure white and hemispherical. The edge of the colony becomes less fluffy and at times is granular. The undersurface of the colony shows the typical rose-purple color which gradually spreads to the edge of the colony and may be noted in varying degrees throughout the colony. Pleomorphism occurs eventually. Under filtered ultraviolet rays (Wood light) the cultures show colors which are bright but hazy. The central half of the colony is mauve, the remainder is a light, soft blue-violet. There are many sterile vegetative hyphae and



Fig. 358.



Fig. 359.

Fig. 358.—Actinomyces, gram stain shows mycelium within a fungus granule. (Dr. Fred Weidman.)

Fig. 359.—Actinomyces, sectioned gram stain shows mycelial filaments which are seen along upper margin of granule. (Dr. Fred Weidman.)



Fig. 360.



Fig. 361.

Fig. 360.—*Sporotrichum schenck*, culture. (Dr. F. W. Sims.)

Fig. 361.—*Sporotrichum schenck*, hanging drop culture, showing trefoil clusters of stipitate conidia. (Dr. Fred Weidman.)

many microconidia in thyrses and in grapelike clusters in culture mount. Fuseaux are few. Chlamydospores develop in older growths. Inoculation of animals is occasionally successful. The index of sensitization is low.

**Trichophyton violaceum (Tinea)**

*Direct Examination.*—Large spores in linear arrangement may be seen in the shaft of an infected hair or in scales or nail tissue.

*Cultural Characteristics.*—The colony is compact, smooth, and shiny, and it has a typical deep violet color. The surface shows convolutions. Pleomorphism is rare.

*Culture Mount.*—The mycelium shows irregular and oddly shaped branches. Few free or attached spores are developed. Chlamydospores are seen in older colonies.

**Trichophyton tonsurans (crateriform) (Tinea)**

*Direct Examination.*—Large spores in chains are seen in the shaft of the infected hair usually in large numbers.

*Cultural Characteristics.*—The growth is compact, creamy white, and velvety. The central portion is broken and depressed, being yellow. Pleomorphism is rare.

*Culture Mount.*—Conidia in clusters (grapes) or on stalks (thyrses) are to be noted. Chlamydospores are common.

**Monilia (Candida) albicans (Moniliasis)**

Colonies originate by bipolar sprouting of blastospores and the pseudomycelium is composed of ellipsoidal cells. The colonies are creamy, thick, and convex. *Candida albicans* is a yeastlike fungus, differing from a true yeast in that a pseudomycelium is formed, whereas true yeasts reproduce by budding, and the daughter cells do not adhere to the mother cell.

*Cultures.*—The growth is smooth, pasty and cream-colored, and it grows rapidly on dextrose medium. The central portion later appears honeycombed. On corn meal agar mycelium, characteristic spore clusters, and chlamydospores develop. Ascospores are not formed.

*Agglutination Reaction.*—The organism agglutinates in a serum prepared against *Monilia albicans* (Benham: J. Infect. Dis. 49: 183, 1931).

*Animal Inoculation.*—Benham (1931) found that the intravenous injection of 1 c.c. of 1:100 suspension of a culture kills a rabbit in 4 or 5 days. Abscesses in which *Monilia albicans* may be recovered develop in the kidneys and other organs.

*Differential Diagnosis.*—Cryptococci do not develop mycelium, and other species of *Monilia* may be distinguished from *M. albicans* by the absence of chlamydospores when grown on corn meal agar. *Mycoderma* may usually be recognized by its gross appearance in culture; a culture mount reveals arthrospores. Endomyces and Saccharomyces form ascospores; the former also develops mycelium.

**Epidermophyton floccosum (inguinale)**

*Direct Examination.*—The scales contain chains of spores in which the elements tend to be flattened. The amount of fungus material is often plentiful.

*Cultural Characteristics.*—After 2 or 3 weeks the growth is apparent. It develops a velvety surface with irregular folds and is characteristically grayish olive drab or greenish drab in color. Pleomorphism develops early.

*Culture Mount.*—Fuseaux of the blunt-end variety are to be seen in groups. Chlamydospores and racquet mycelium may also be observed.

**Malassezia furfur (Microsporum furfur) (Tinea versicolor)**

*Direct Examination.*—Fungus elements are usually present in profusion and the picture is characteristic. They consist of round or ovoid, refractile spores in clusters. Mycelia, fairly long but fragile, occur in considerable numbers.

*Cultures.*—Doubtfully successful. See Tinea versicolor.

**Nocardia minutissima (Actinomyces minutissimus) (Erythrasma)**

*Direct Examination.*—On examination with the high power of the microscope, fine threads may be noted. If the oil-immersion lens is used, the threads are visible, being long, tortuous, and interlacing. A few spores may be seen.

*Cultural Characteristics.*—There is not general agreement that this microorganism has been cultured.

**Trichophyton concentricum (Endodermophyton tropicale) (Tinea imbricata)**

*Direct Examination.*—Numerous segmented hyphae are noted.

*Cultural Characteristics.*—The growth is compact and gray to brown in color and it shows an uneven surface. Superficial resemblance to *Achorion schoenleini*.

*Culture Mount.*—Vegetative forms may be noted. Microconidia are not present.

**Actinomyces bovis (Actinomycosis)**

*Direct Examination.*—This is the most important laboratory investigation of a patient suspected of infection with this microorganism. The granule is seen to consist of one or more colonies in which in the mid-zone there is a mass of twisted mycelium, and at the periphery a palisaded arrangement of hyphae, forming a fringe. These latter strands are enlarged at one end and are striated. The ray fungus is gram-positive. The central mycelium takes the basic dye and the peripheral zone takes the acidic dye.

*Cultural Characteristics.*—There is considerable difficulty in obtaining a cultural growth, and it usually dies quickly. The colonies are pasty but of variable consistency and configuration.

*Culture Mount.*—Sterile mycelium without characteristic spore forms.

**Monosporium apiospermum** (Maduromycosis)

*Cultural Characteristics.*—Rapidly growing colony producing a white, cottony aerial mycelium which later turns gray or becomes buff to brown in color is found.

*Cultural Mount.*—Ovoid and pyriform conidia, 8 to 10 microns long by 5 to 7 microns wide, are produced singly at the ends of long conidiophores or from the sides of the mycelium on short conidiophores.

**Rhinocladium (Sporotrichum) schenckii** (Sporotrichosis)

*Direct Examination.*—Cigar-shaped cells may be noted, but fungus material is usually absent.

*Cultural Characteristics.*—After 2 weeks, a moist growth is noted which is light brown in color but with ge it becomes dark brown. The central portion shows irregular foldings. White excrescences form on the surface.

*Culture Mount.*—Pear-shaped conidia are situated irregularly along the mycelium and arranged also as terminal triads and tetrads.

**Blastomyces dermatitidis** (Blastomycosis of Gilchrist)

*Direct Examination.*—Single budding, thick walled, round or oval, granular cells, 8 to 20 microns in diameter are to be found.

*Cultural Characteristics.*—The central portion of the colony is gray and smooth, becoming white and filamentous. A peripheral moist zone is usually present. Yeastlike growths are obtained on blood agar.

*Culture Mount.*—Microconidia, chlamydospores, and racquet mycelium may be noted. Budding cells may be obtained from the yeastlike growth.



Fig. 162.

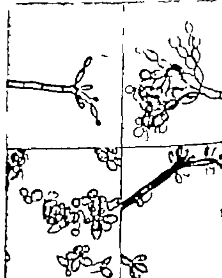


Fig. 163.

Fig. 162.—Tinea. KOH preparation of a scale.

Fig. 163.—*Hormodendrum pedrosoi.* *Above* Dendroid pore heads from corn meal agar slide culture. *Lower left* spores dissociated from conidiophore. *Lower right* crothecal type of sporulation (Emmons, Hailey nd Hailey J 116 25, 1941)

**Coccidioides immitis** (Blastomycosis of Rixford and Gilchrist)

*Direct Examination.*—The microorganism is a sphere with doubly contoured capsule from 5 to 60 microns in diameter, and it contains 6 to 20 endospores.

*Cultural Characteristics.*—The growth is white and filamentous browns h shade develops with age.

*Culture Mounts.*—Septat mycelium is profuse. Arthrospores and chlamydospores may be distinguished.

**Cryptococcus neoformans (T rula histolytica)** (Torulosis)

*Direct Examination.*—V rious-sized budding cells will be seen. A wet India-ink preparation reveals a wide capsule.

*Cultural Characteristics.*—The colony is moist and cream-colored, l ter changing t yellow nd then t brown.

*Culture Mount.*—Round or al, various-sized budding cells will be seen (India-ink technic) N mycelium and no ascospores will be found.

**Bl stomyces brasiliensis** (South American Blastomycosis)

*Direct Examination.*—Single nd multiple budding, thick walled yeastlik cells, 10 to 60 microns in diameter are found.

*Cultural Characteristics.*—Slow-growing, heaped, membranous or wrinkled colony with a short nap of white aerial mycelium which tends to become brown with age.

*Culture Mount.*—A few sessile, oval to round conidia may be seen in culture at room temperature. Single and multiple budding, yeastlike cells may be seen in culture at 37 C.

**Hormodendrum pedrosoi** (Chromomycosis)

*Direct Examination.*—So-called sclerotic cells (Medlar) are present. These may be septate and are usually in groups. Small septate filaments may also be noted.

*Cultural Characteristics.*—The growth is compact, limited, and felty. Concentric zones may be colored brownish olive, olive black, olive gray and grey.

*Culture Mount.*—Olive brown spores are borne on conidiophores. Disjunctors are also usually present.

**Phialophora verrucosa** (Chromoblastomycosis)

*Direct Examination.*—Single or clustered, round, thick-walled, dark brown bodies which multiply by splitting and not by budding. It is not distinguishable from Hormodendrum pedrosoi.

*Cultural Characteristics.*—Slow-growing colonies, dark brown in color, are found.

*Cultural Mount.*—Conidia arising from cups at the tip of flask-shaped conidiophores borne terminally or laterally, singly or in groups, on the aerial mycelium are found.

**Rhinosporidium seeberi** (Rhinosporidiosis)

*Direct Examination.*—Round to ovoid spores, 7 to 9 microns in diameter and spore-filled sporangia are found.

**Pityrosporum ovale.**

*Direct Examination.*—Flask-shaped cells of 3 to 10 microns, with or without budding, are seen. See seborrheic dermatitis, p. 334.

**Demonstration of Fungi.**—One extracts a whitish hair stump or tears off the cap of a blister and immerses this in 10 per cent aqueous potassium hydroxide. After maceration the bit is crushed under the cover slip and dim light is used in examination. Experience is necessary for distinguishing hyphae and spores from droplets of fat, epithelial cells, and detritus. Fungi may be stained (Swartz and Conant ADS 33 291 1936). Mosaic fungus, so-called, is perhaps not fungus at all, for it dissolves in ether, absolute alcohol, and phenol. It seems to be a degeneration product (Dowding and Orr ADS 33 865 1936).

## TINEA

**Symptoms.**—Tinea ( ringworm ) is infection of the skin, hair or nails produced by various fungi. Such infections are common and are at times serious. The ability of dermatophytes to grow on keratin forms the basis of their parasitic relationship with the human host. Sensitivity to dermatophytin in superficial mycotic infections, as well as in deep ones is almost constantly present. There are analogies between the immunologic biology of dermatomycosis and of tuberculosis. Infectious diseases in general are characterized by the appearance of a primary lesion at the site of inoculation and by the appearance of lesions of the skin under allergic conditions. Such latter dermatoses comprise the ids. Allergy is the sine qua non of their existence. During the existence of a trichophytid the trichophytin reaction is positive.

Environmental circumstances influence the equilibrium of the parasitic relationship so that the fungus may thrive or the tissues prevail. Moisture, warmth, darkness, and traumatic or chemical irritation favor the fungus. Ventilation, coolness and dryness favor the tissues, as, of course do débridement (washing), avoidance of injury and nonirritating antiparasitic chemicals. Eczematous tinea is sometimes the equivalent of dermatitis venenata due to a self reproductive chemical substance. Clinical disease is often a composite representative not only of fungus infection but, in addition, of chemical damage from contactants including medicines, secondary infection and even focal bacterial infection.



Fig. 364.—Tinea corporis: concentric rings of inflammation.



Fig. 365.—Tinea corporis.



Fig. 366.—Tinea of axilla.



Fig. 367.—Tinea cruris (eczema marginatum).

Fungi which are principally pathogenic to animals cause in animals lesions which are not very deep and inflammatory disease which is readily transmissible from animal to animal, lesions which contain numerous organisms easy to demonstrate lesions which are difficult to cure. The same organisms in the human being produce deeper and more inflammatory lesions, strong reactivity to trichophytin, disease which is not readily transmissible lesions in which organisms are few and demonstrable with difficulty and lesions which tend toward spontaneous cure or are comparatively easy to cure. Fungi which are principally pathogenic to human beings cause chronic, resistant noninflammatory disease in human beings and in animals cause deeply inflammatory lesions. The distinction between animal and human infections is only a rough distinction.

**Tinea Corporis.**—Tinea of the glabrous skin usually begins as a flattened reddish papule The lesion tends to spread peripherally and to *heal in the center The central portion is pinkish and has a superficially* scaling surface. The margin is sharply defined slightly elevated, actively inflamed, more or less scaly, and often vesicular in places. Circinate lesions gradually enlarge. Occasionally patches coalesce, giving rise to arcuate figures. They may disappear spontaneously leaving no trace The tendency to undergo central involution is lacking in some cases, so that the eruption may consist of solid reddish, scurfy oval patches. Concentric rings of activity are common. The lesions range in number from a few to a dozen or more Itching or burning of slight degree may be present, but symptoms are seldom prominent The sites of predilection are the uncovered surfaces. Palms are sometimes attacked, and tinea often affects soles and interdigital skin fingers and hands being involved secondarily Mucous membranes escape. Perianal skin is often involved, and tinea constitutes one cause of pruritus ani Mycotic vulvovaginitis is usually monilial. Diagnostic differentiation from pityriasis rosea, seborrheic dermatitis, and psoriasis rests on demonstration of fungi in the scales.

**Tinea Cruris** may occur also in the axillae or beneath pendulous breasts It is usually due to *Epidermophyton inguinale* Usually the primary eruption consists of a few superficial, circinate patches which sooner or later coalesce to form confluent, symmetric bat wing-shaped inflammatory areas which have sharply defined, elevated borders. The patches are generally located on the inner surfaces of the thighs, contiguous with the scrotum or labia and the intergluteal regions Extensions along the sagittal line anteriorly and posteriorly give rise to involvement of the mons veneris and the perianal region and intergluteal fold About the anus and over the coccyx fissuring is likely to occur and chronic pruritus results. The lesions of tinea cruris are usually moist at first and they readily become macerated, secondarily infected and painful as well as merely itchy As they heal they become dry scaly and less edematous. Recurrences are common, for friction, sweating tight clothing and obesity combine to favor luxuriation of the organism Tinea of the feet and nails commonly serves as the source of reinfection. Crural dermatomycosis due to *Blastomyces* is vegetative and papillomatous. Any of several species of fungi may infect this region In monilial vulvovaginitis mycotic dermatitis of the near-by skin is likely to be present Tinea of the crotch in women calls for an examination of the vaginal secretions and for the use of douches, such as 1 5 000 potassium permanganate on general principles. In erythrasma the patches are superficial and only slightly inflammatory

**Tinea of the Hands and Feet.**—*Epidermophyton Trichophyton Monilia albicans* and other organisms are active here Tinea of the hands often depends on the existence of tinea of the feet or nails. Dermato-





Figs 368 and 369 —Tinea of feet. (Dr Wende.)



Fig 370



Fig 371

Figs. 370 and 371 —Not all dermatitis of the feet is tinea. Fig. 370 is a secondary syphilid. Fig. 371 is pustular psoriasis. (Dr Royal M. Montgomery.)

phytids of the hands are more common than demonstrable tineal infection. Tinea-like pompholyx can be cured by applying treatment to the feet or to some other focus. Streptococcic and staphylococcic dermatitis of the hands, recalcitrant perhaps because of focal infection, is likely to be the correct diagnosis when the hands alone are painfully inflamed in the absence of lesions of the feet (Mitchell ADS 10 659 1920 see p 162)

Three varieties of cases are seen (White JOutD 87 501, 794 1919)

VESICULAR, in which the lesions are grouped and are accompanied by marked itching, being characterized by sago-grain vesicles and occurring preferentially in warm, humid weather;

SQUAMOUS, resembling scaling dyshidrosis, usually with a central primary lesion which results from the drying of confluent vesicles and

PUSTULAR, resulting from secondary infection.

The essential lesions are vesicles, and these are deeply seated, only slightly elevated and resemble boiled sago grains embedded in the epidermis. The content is usually clear and as a rule there is no erythema surrounding new vesicles. Within a few days the fluid is absorbed leaving a brownish macule. Eventually the roof of the dried vesicle becomes torn, exposing a red, smooth, shiny surface with a collarette of upturned scales. In acute cases the vesicles may be grouped and may become confluent, even forming bullae. When vesicles are grouped in a dry area such as the palm or sole, desquamation occurs, leaving a circular well-defined, shiny reddish area denuded of corneum. This may heal spontaneously or new vesicles may continue to develop about the periphery Fissures may occur beneath the flexural folds of the toes. Maceration of exfoliated epidermis in the fourth interspace produces a white, sodden, thickened, adherent mass of epithelium. Hyperhidrosis is usually an associated symptom. The patient s complaint is of itching which may be moderate or severe. Pain and incapacitation occur in acute, bullous cases (Ormsby and Mitchell J 67 711 1916) especially when pathogenic cocci add their effects to the situation.

**Trichomycosis (Tinea of the Hair)** —Fungi parasitizing hair include microspora and trichophytons. Microsporum infections are described in following paragraphs under Tinea Capitis. Trichophyton infections were long classified as endothrix and ectothrix, indicating predilection of the fungi for growing respectively within the hair shaft or on it.

Endothrix parasites of importance are *T violaceum* *T sulfureum* and *T crateriforme* (Levin and Behrman J 128 850 1945) *T violaceum* causes black dot ringworm so called because infected hairs split off close to the scalp in scattered patches. All three endothrix fungi provoke usually a clinical picture characterized by follicular pustules and small eczematoid patches. Wood s light reveals usually a dull white fluorescence, exceptionally a bright white fluorescence confined to individual hairs and so distinguishable from the glisten of medication, which is widely dispersed and can be wiped off with carbon tetrachloride. The KOH preparation shows large spores usually in chains throughout the hair shaft *T violaceum* lesions are likely to result in cicatricial alopecia. *T violaceum* is the organism most frequently found in tinea of the scalp in adults in Peiping (Mu and Kurotchkin ChinMJ 55 201, 1939)

Ectothrix parasites are uncommon invaders of the scalp The two important ones are *T gypseum* and *T purpureum*. The former usually

produces pustular inflammation and kerion. Wood's light reveals no abnormality of fluorescence. The microscope shows chains of spores external to the hair shaft. Clinical resemblance to *M. lanosum* infection is close but the lack of fluorescence should arouse suspicion. Diagnosis requires cultural identification. *T. purpureum* rarely involves the scalp.



Fig. 372.—Tinea capitis, "human" type, after roentgen epilation. (Dr. MacKee.)



Fig. 373



Fig. 374

Fig. 373.—Tinea capitis: section of infected hair showing strand of fungus within shaft and perifollicular inflammation. (Dr. Fred Weidman.)

Fig. 374.—Kerion, showing fungus in hair and intense inflammation. (Dr. Stuart Way.)

**Tinea Capitis** is usually a disorder of childhood. The earliest lesion is a small rounded, scaly patch or a red papule perforated by a hair. The dermis is somewhat hyperemic, but the surface is scaly and whitish or grayish in color. As the patch slowly widens, it shows no tendency to undergo central involution. Hair shafts become dry, lusterless, whitish and brittle. They break off and so occasion one variety of symptomatic alopecia. The patches range in size up to several centimeters in diameter and they may coalesce. Itching is the principal symptom, and scratching may lead to secondary infection. Tinea capitis in children is an infectious, often seriously epidemic disease of consequence to economy and education. It is transferred by barbers, the initial infection in the site cut by clippers, as well as by immediate contact from child to child (Schwartz et al. J 132 58 1946). Children are susceptible to infection while most adults are not. Extract from children's hair was more favorable as a culture medium than from adults, reported Kingery et al. (ADS 40 879 1939) and Rothman and Smiljanic (Sc 104 201 1946) showed that this is due to the relatively high concentration of fungistatic free fatty acids of 5 7 9 11 and 13 carbon atoms in adults' hair. The fat of adult hair containing normal aliphatic monobasic acids with an odd number of carbon atoms, does not kill fungus spores in hair but prevents their infecting new hairs which replace infected ones in the process of shedding (Rothman et al. JInvD 8 81 1947).

*Microsporum lanosum* produces well-defined patches of alopecia with marked inflammatory reaction consisting of erythema, scaling, pustulation and crusting and this may lead to spontaneous cure. It also produces lesions distinguishable from those of *M. audouini* only by cultures.

*Microsporum audouini* infection is not so intensely inflammatory, produces gray scaly patches and is generally less readily curable. *M. audouini* infections are in fact so resistant that roentgen epilation is often but not always required, while in other types of infection local applications alone are likely to suffice.

Diagnostically typical are the partly bald, well-defined, scaly areas marked by lusterless and brittle or broken hairs and dilated or débris-stuffed follicular orifices. One must distinguish seborrheic dermatitis, favus, contact dermatitis, infectious eczematoid dermatitis, and alopecia areata. In alopecia areata infected hairs are absent, the bald region is in no way inflamed, and the circular patch of bald scalp is not scaly. Microscopic and cultural examinations are requisite.

A broken, whitish stub is extracted with an epilating forceps. It is placed in a drop of 10 per cent potassium hydroxide solution on a glass slide and after a few minutes it is examined under the microscope. Fungi are ordinarily easy to find if they are present and a fruitless careful search is one criterion of cure.

Wood's Light is ultraviolet light comprising wave length of about 3650 Å which passes a Wood's filter made of glass containing nickel oxide. Exposed to this light in a dark room, infected hair stumps fluoresce and can quickly be differentiated by their bright clear bluish green appearance when infected with *Microsporum*. Since this is the usual pathogen, the test is practical (Lewis and Hopper ADS 34: 644, 1936). It affords a rapid and invaluable means for surveying numbers of children and identifying the infected ones.

Lepothrix (trichomycosis, which may be yellow, black or red) is a dermatomycosis characterized by the occurrence of firm concretions on hairs or by soft sheaths surrounding them. The axillary hair is commonly involved and adjacent skin is often infected. Concretions on the hairs, yellowish or reddish in color, are composed of masses and chains of microorganisms, embedded in a homogeneous chitin-like sub-

stance Species of *Actinomyces*, mingled with certain cocci, are the cause (Lane JCutD 27: 88 1919) The disorder can be cured by washing with benzine and applying 1 1,000 alcoholic solution of mercuric chloride. The hair should be shaved.

**Piedra** is a disease of the hair seen in some districts of South America. It is characterized by the development of dark, nodular pin-point to pin head sized, gritty masses on the shafts of the hairs of the scalp, eyelashes or beard (McCarthy J 123: 419 1943)

**Tinea Amiantacea**, asbestos-like tinea, i a disease of the scalp. Hea y scales extend onto the hairs binding together the hair shafts. It may be circumscribed or diffuse. It i chronic. It is not followed by atrophy scarring or alopecia (Becker and Muir ADS 20 45 1929) The condition was interpreted as a symptom complex which may occur in neurodermatitis or psoriasis, and is responsive to an ant

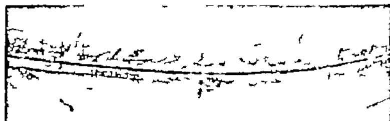


Fig. 375.—Lepothrix. (Dr Harris)

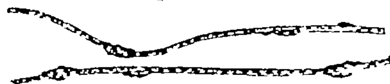
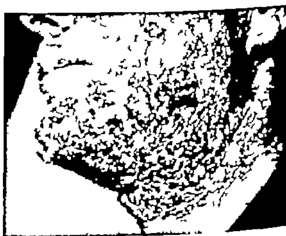


Fig 3 6—Piedra in olving hair of Indian girl of British Guiana. (Macleod BJD 24 132, 1912)



Fig 3



F g 378

Fig 377 —T nea of hairy skin, h g spore animal type minat folliculitis (Dr M. L. Heidingsfeld.)

Fig. 378.—Tinea barbae kerion. (Dr J A. Robertson)

ment containing 5 per cent each of salicylic acid and oleate of mercury and to small doses of x ray therapy (Brown: BJD 60 81, 1948) Brown preferred the name Pityriasis amiantacea believing that fungi are not causative.

**Tinea Barbae.**—SUPERFICIAL TYPE.—Infection may involve several hair shafts to a greater or less extent but seldom to the extent seen in tinea capitis Infected hairs become dry and brittle and can usually be extracted readily the diseased root-sheath often adherent to the shaft. There are more or less infiltration, scaling and itching Vesiculation and pustulation are commonly absent. The disease frequently remains superficial throughout its course.

DEEP TYPE.—Deep involvement characterizes many cases, either from the beginning of the attack or after the disease has been present for several days in superficial form. The lesions may be few or many Numerous, disseminated lesions constitute **sycosis** as distinguished from **kerion**, in which the lesions are large carbunculoid, and few These inflammatory tumors are flat or oval and reddish, and are studded with dead or broken hairs or with gaping follicular orifices. Such nodules may ulcerate in the center but ordinarily pus and seropurulent material are discharged through inflamed, dilated, follicular openings. The common site for the lesions is the skin beneath the jaw and in the cervicomaxillary fold. As a rule the upper lip escapes. This inflammatory form of tinea barbae usually exhibits a tendency to undergo self-healing

Kerion may be caused by any of several different fungi, including *M lanosum*, *M audouini* *M fulvum*, *T gypseum*, *T niveum*, and *T crateriforme*. Cultures are best obtained from the pus. After an average duration of 6 to 8 weeks, the hair may be expected to regrow (Layman MinnM 29 137 1946) and while expectant treatment is sufficient, manual epilation may help

Kerion of the scalp is like kerion of the beard. Similar carbuncular lesions on the dorsum of the hand or forearm may be called agminate folliculitis.

**Suppurative Tinea** is a name designed to include kerion, sycosis and agminate folliculitis. Variants of *Trichophyton gypseum* are the usual offenders. Many such cases occur in people who handle cattle. The trichophytin test is usually positive in suppurative tinea. Fowle and George (ADS 56 780 1947) reported 23 cases contracted from cattle and due to various trichophytons.

Granuloma Trichophyticum is a type of deep ringworm differing from kerion chiefly in its chronicity and its milder degree of inflammatory intensity It does not suppurate until late or unless it becomes secondarily infected. It occurs on the scalp and beard in connection with pre-existent fungus infection, and on the dorsa of the hands, forearms, and feet. The lesions are sharply defined and have smooth surfaces. They may persist for months or years. Sometimes they are acutely inflammatory sometimes hard and keloid like with deformed hairs at the periphery They may occur on the leg and are readily mistaken for erysipelas, lichen chronicus simplex, or stasis dermatitis.

**Tinea of the Nails.**—*Trichophyton gypseum* and *T purpureum*, as well as *Candida albicans* and the organism of favus, are the parasites which commonly attack the nails (Rockwood ADS 22 395 1930) They are capable of living in the nail substance, which they invade more or less deeply—*Trichophyton purpureum* attacks especially deeply—and so they cause the nail to become thickened, lusterless, friable, and whitish or yellowish in color Progress of invasion toward the nail root exceeds the rate of nail growth so that eventually the entire nail plate may be supplanted by a scaling and horny malformed, infected mass. The surface

layers of the nail plate may be preserved while soggy stinking material accumulates beneath it or the plate may exfoliate as far proximally as the invasion of its deeper layers has progressed Nails may be primarily involved, or secondarily to cutaneous infection. Chronic interdigital tinea of the feet eventuates in infection of the nails almost invariably When *the nails have become infected, they serve as foci responsible for the dissemination* of parasites and for repetitions of ids.

Invasion of the nail is gradual. The free extremity of the nail particularly at the side, first is involved. Several nails may be infected, but the times of onset are separate Sharply demarcated patches of opacity on and within the nail substance asbestoslike and angulated in outline are known as leuconychia trichophytica There may be no inflammatory paronychial disease The organisms are on and within the nail plate and are readily demonstrable



Fig 379.—Tinea of nails leuconychia trichophytica.



Fig 380 Fig 381. Fig 382.

Figs. 380 381 and 382.—*Trichophyton purpureum* infection of glabrous skin, toenail fingernail (Lewis et al ADS 37 623 1938.)

**Mycotic Paronychia.**—The paronychial tissues are susceptible to fungus infection, although many a rebellious paronychia is bacterial and dependent upon focal infection The disease may be acute subacute or chronic Inflammation maceration vesiculation, and fissuring between and about *the fingers frequently are concomitant The disease tends* to be an occupational one, affecting individuals exposed to pathogenic fungi while their hands are wet at work (Kingery and Thienes ADS 11 186,

1925) Manicuring may serve to inoculate the infection *Candida albicans* is the usual cause. In treatment, avoidance of long-continued moisture is important Gentian violet is useful. Soaks in 1:5 000 potassium permanganate and a paste of sodium perborate are excellent measures. Roentgen therapy helps.

**Otomycosis and Myringomycosis.**—Many fungi are capable of provoking integumentary inflammation in the external auditory canal. Itching and impedance of hearing result. On the tympanum the parasites form *a coating of mycelium of blotting paper like consistency and bad odor* Many different organisms can cause otomycosis. Branny desquamation or moist exfoliation with oozing is seen

Otomycosis and myringomycosis do not undergo spontaneous resolution. They generally respond favorably to mild antiseptics along with careful débridement. Recurrence is likely Ten per cent salicylic acid in 70 per cent alcohol may be dropped into the canal. Silver nitrate solution may be swabbed over the affected skin. Metacresyl acetate has been highly recommended (Whalen J 111 502, 1938 Rech AnnOtol 51 146, 1942, adds 1 per cent thymol) Sodium propionate 8 per cent in propyl alcohol for swabbing twice daily followed by insufflation of 10 per cent sodium propionate in talc, was the recommendation of Duemling (ADS 52 75 1945) A wick moist with saturated aqueous solution of boric acid may be kept in the canal. Gentle and expert débridement is helpful.

**Dermatophytid.**—In mycotic infections there may occur widespread, disseminated eruptions due to allergy to fungi (Low BJD 36 432, 1924) Dermatophytid is the general name for such eruptions, which differ widely in their clinical forms. *Epidermophytid, moniliid* and *trichophytid* are specific names, applicable when the specific causative agent is known The incubation period is about ten days. The eruption may follow x ray or trichophytin treatment It may be violent or mild. During it, the specific test is always positive and is generally accompanied by focal flare. It occurs when the primary site is actively vesicular or inflammatory

**Types of Dermatophytids.**—Lichen trichophyticus the name applied to a dermat phytid occurring in ti ea f the scalp in which th eruption is composed of scant or numerous, small red papules located on the back and shoulders, becoming scaly as they disappear Dermatophytic erythema multiforme and erythema nodosum have been seen. The commonest dermatophytid pompholyx (p. 96) of the hands in vesicular tinea of the feet (Peck: ADS 22 40 1930) If the focus is not controlled, the eruption may pread to involve the arms in scattered, discrete and confluent patches f erythema, later becoming eczematou and scaly The sides of the neck and the face may become involved. Erysipela like, recurrent dermatitis of the lower extremi ties was recognized a n id by Traub and Tolmach and by Sulzberger et al. (J 108 2187 189 1937) I flammatio less t nse and more diffuse than in erysipelas. The lesions recur in patches of constant size shape and location, as fixed drug eruption do, noted Wassman (ADS 53 10 1946) His patient manifested the usual immediate wheal reaction when trichophytin wa injected within the area of the lesion. *Hyposensitization was not successful when allergin wa injected into normal skin but was when injected within the lesion, following which the immediate reaction was reduced but not the 48 hour type f reaction.* Passive transfer of reactivity was demonstrable as is usual, in Wassman carefully studied patient in whom specific hyposensitization wa obtained despit the persi tence f positi skin *reactivity and of* Prausnitz Küstner reagins

Dermatoph tids re free from demonstrable fungi. They depend on hyperergy to produ t of fungi. Dermatophytid tend to occur in bowers and to disseminate symmetrically and the blood culture may be positiv (Peck JIndianaMA 37: 304, 1944) Injections f trichophytin nat the skin regularly reduce sensitivity and increase tolerance and hyposensitization so produced is sometimes accompanied by clinical improvement, but there is seldom satisfaction in *treating tinea and its allergy by*

means of trichophytin. One does better to attack the foci with appropriate means and, in treating the *ids*, to use bland, nonspecific remedies such as 1:500 aluminum acetate for wet dressings or calamine lotion with phenol.



Fig. [illegible].—"Keratolysis," a common type of dermatophytid usually due to dermatomycosis of the feet. (Dr Wende.)



Fig. [illegible]



Fig. [illegible]

Fig. [illegible].—Vesicular dermatophytid such as may result from pedal epidermophytosis (compare pompholyx).

Fig. [illegible].—Dermatophytid resembling urticarial erythema multiforme in a patient with vesicular tinea of the soles.

**Dermatomycins.**—Vaccinal preparations of fungi have been studied with regard to their academic and practical significance. Reactions to trichophytin include the immediate urticarial reaction, the late tuberculoid inflammatory reaction to intradermal tests, and the eczematous reaction to patch tests. Efforts to obtain practical therapeutic results by the use of vaccinal agents may summarily be adjudged fruitless. Precipitins, agglutinins and complement fixation antibodies circulate in human beings who are hypersensitive to dermatomycins. Thus vaccinal fungus materials can be used in diagnosis much as tuberculin and luetin are used. Again the practical importance is slight because allergy from past infections, presently unimportant, may persist so that a positive test has no trustworthy significance as to the nature of the dermatosis at hand (Lewis and Hopper: ADS 38: 713, 1938).

**Etiology.**—Mycotic infections of the skin are common disorders. Moisture, warmth, and darkness are predisposing environmental circumstances. Infection may occur immediately or through contact with contaminated articles such as towels, slippers and bath mats. Mycotic infections of animals are readily transferred to human beings, sources being cats, dogs, horses, cattle and even birds. Epidemics are commonplace, and schools, armies, and other communities where personal contact is close are subject to them. There are individual differences in susceptibility to infection, but lasting immunity apparently develops in no one, and reinfections are common. See tinea capitis, p 307

**Prognosis.**—The outlook in mycotic infection varies with the location, extent, duration of the disease, the specific cause and the reactivity of the particular patient. Tinea corporis usually responds readily and favorably to treatment, although *T purpureum* infections are exceptions to this rule. In extensive cases of tinea of the scalp the infection is extremely rebellious in some cases, easier to cure in others, depending on the infecting organism. In cases in which kerion occurs baldness due to scarring may result. Great care must be exercised in examining a case before discharging it as cured. Good treatment, which implies attention to detail and to the following of correct broad principles, is materially advantageous. In recent military experience, a wet tropical climate rendered cure without evacuation sometimes impossible. All infected areas must be treated simultaneously so that dissemination cannot occur Fungi like bacteria, propagate fast under suitable conditions. Animal and human sources of reinfection along with inanimate sources, such as clothing and shoes, must be recognized and dealt with. Dermatitis venenata due to medication must be recognized and avoided. Secondary coccic infection is commonplace, and focal infections must be eradicated in many a patient before cure of what appears to be chronic tinea of hands or feet can be achieved.

**Treatment of Tinea.**—Correct diagnosis is essential. The distinction of tinea from dermatitis venenata and from coccic disease is important. Tineal dermatitis is due to moldlike fungi which primarily parasitize the dead horny cells of the epidermis and secondarily provoke inflammation, allergy eczematous dermatitis, and antibody production In the places in which the living fungi are present, treatment is aimed at (1) their mechanical removal and (2) chemical destruction of them. Violent chemical measures are seldom one's first choice. In the lesions due to allergy, the aims are (1) attacking foci whence dissemination originates and where fungi are present (2) soothing the inflamed skin where pathogenic fungi are not present so as to give the patient symptomatic relief Many chemical substances are serviceable, and none of them is specific (Kingery et al. JLCM 20 0.0 1935) The physician's job consists not in extermination of parasites but rather in tipping the equilibrium between host and parasite in favor of the host, while one trusts to the natural responses to attend to the healing The antitheses of moisture, warmth, and darkness are prescribed, while suitable débridement may deprive the parasite of its cultural medium. Vesicles should be opened so that chemicals can get into them. In acute, vesicular lesions, astringent soaks and antiseptic powders are serviceable. Inflamed skin treated with soaks and without grease readily becomes cracked and fissured if it is flexed, but it regains its normal flexibility when the inflammation disappears. The

use of unguents, while comforting is here likely to disappoint. Medicines must be stopped before they do harm. The plan of treatment must be individualized.

Obesity predisposes to mycotic infections. In diabetes the sweat is laden with sugar which serves as pabulum especially for *Monilia*. Tight clothes keep the crural regions continually moist and ill ventilated so that tinea of the crotch may be impossible to cure until these conditions have been altered. Shoes which are tight across the toes, holding them in continuous juxtaposition make it next to impossible to cure interdigital tinea.

Constitutional remedies are of no value. Arsphenamines are decidedly dangerous as well as useless, for the sensitivity of the skin is precarious during mycotic infection. Vaccinal therapy has been disappointing.

Roentgen therapy in treating tinea must be used with greater wisdom than in most other conditions for which it is useful. X ray energy does not kill the fungus. Roentgen therapy stops hyperhidrosis, provokes dissolution of inflammatory reaction and helps to cause vesicles to resorb (Brundage SMJ 31 1297 1938). It inhibits the ability of the skin to respond to the presence of the fungus, and its use is generally followed by several days of remission. When roentgen therapy is used time after time as the disease repeatedly reappears, the result is atrophy or burn. We find roentgen therapy seldom desirable.

**Chemical Agents We Consider Most Useful Are**

Soap and water along with a scrubbing brush sometimes, and perhaps reinforced with sand paper for attacking thick collection of scales in chronic squamous tinea of the feet.

Soaks or compresses such as

1:3,000 potassium permanganate
℞ Potassium permanganate — — — — — 0.0
Water — — — — — — — 100.0
Sig. 1 teaspoonful to 1 qt water for soaks, douches, or compresses.

1:10,000 bichloride of mercury
℞ Bichloride of mercury — — — 1.0
Water — — — — — — 10.0
Sig.: POISON 1 teaspoonful to 1 qt water for soaks or wet packs.

1:500 aluminum acetate
℞ Aluminum acetate powder — — — 2.0
Put equal portions into 10 capsules
Sig. 1 capsule to 1 pint of water for moist packs.

Chrysarobin 3 per cent dissolved in chloroform, especially serviceable on the nails after débridement and on dry superficial tinea of crural or axillary folds, between the toes, or (with caution—it is hot!) about the anus.

Five per cent silver nitrate in water for occasional topical application serving as a protein precipitant capable of rendering the epidermis uninhabitable.

Tincture of iodine for painting infected nails.

Salicylic acid 3 per cent in 1:1,000 tincture of merthiolate is useful for chronic vesicular tinea. The 10 per cent alcoholic solution of salicylic acid is popular.

Gentian violet per cent aqueous solution, is fungicidal for gram positive organisms, not toxic and astringent.

A dusting powder such as
℞ Camphor — — — — 1.0
Salicylic acid — — — 1.0
Zinc oxide
Cornstarch
Zinc stearate — — — of each to make 100.0
Sig. Dust between toes and into shoes to keep feet dry.

Desenex powder a proprietary undecylenic acid preparation, recommended in interdigital and intergluteal or crotch infections.

Ethyl chloride spray defatting desquamative, rubefacient (Lewis and Morginson ADS 50 243, 1944)

Whitfield's ointment, a medicament which provokes scaling and which must sometimes be diluted:

| | | |
|---|---|---|
| ℞ | Phenol | 0.3 |
| | Salicylic acid | 1.8 |
| | Benzoic acid | 3.6 |
| | White petrolatum | to 30.0 |

Sig.: Full strength Whitfield's ointment may be diluted with petrolatum. Sulfur 5 per cent may be added.

Schalek paste, an excellent antiparasitic agent:

| | | |
|---|---|---|
| ℞ | Phenol | 0.3 |
| | Salicylic acid | 1.2 |
| | Precipitated sulfur | 1.8 |
| | Zinc oxide | |
| | Cornstarch | of each 4 to 8 |
| | White petrolatum | to 30.0 |

Sig.: Rub in twice daily wash off with soap once daily

Dennie's ointment, a potent mercurial analogue of Whitfield's

| | | |
|---|---|---|
| ℞ | Red sulfide of mercury | 0.1 |
| | Salicylic acid | 3.0 |
| | Benzoic acid | 6.0 |
| | Sulfur precipitated | 2.0 |
| | Lanolin | 20.0 |
| | Petrolatum | 60.0 |

Sig. Dennie orange ointment for fungus infection.

Castellani's fuchsin paint a valuable parasiticidal lotion

| | | |
|---|---|---|
| ℞ | Basic fuchsin, sat. alcoholic sol. | 10.0 |
| | 5 per cent aq. sol. phenol | 100.0 |
| | Boric acid | 1.0 |
| | Acetone | 5.0 |
| | Resorcinol | 10.0 |

Filter

Sig. Apply by swabbing several times a day

There are few cases of tinea which will not respond to one or a combination of these agents correctly used. Medicaments may incorporate the following parasiticidal agents in the percentages indicated

Ammoniated mercury (1 to 10 per cent) parasiticidal, often irritating
Benzoic acid (5 to 15 per cent) antiseptic and scaling
Betanaphthol (2 to 10 per cent) parasiticidal.
Chrysarobin (1 to 10 per cent)—dangerous about the eyes—potent, exfoliative rubefacient reducing agent Dihydroxyanthranol may be substituted
Crude coal tar (2 to 50 per cent) in lanolin and petrolatum, messy but effectively antiparasitic and rarely irritating
Iodine, the tincture—incompatible with sulfur and mercury—antiseptic.
Phenol (1 per cent) antipruritic
Resorcinol (2 to 10 per cent) similar to salicylic acid.
Salicylic acid (2 to 10 per cent) provocative of desquamation; not strongly antiseptic itself
Sodium thiosulfate isotonic to saturated solutions weakly antiparasitic, sometimes irritating, usefulness overestimated.
Sulfur (2 to 15 per cent) excellent fungicidal agent activity enhanced by combination with salicylic acid.
Thymol (0.5 per cent or weaker) fungicidal, liable to irritate

## References on Some Fungicidal Agents

Camphor Phenol (Glen and Hailey ADS 47:229, 1943, unfavorable; Phillips BJD 56:319, 1944, favorable)
Clavicin (Herrick ProExpB 59 41, 1945; 0.5 per cent topical, lethal to pathogens)

Common Ion Transfer $CuSO_4$ Iontophoresis (Greenwood and Rockwood: ADS 44:104, 1941)
Ethyl Iodide Inhalation (Swartz ADS 40:962, 1939)
Evaluation of Fungicides (Weidman et al J 128 803, 1945)
Fatty Acid Therapy.—Sulzberger and Kanof (ADS 55:391, 1947) Muskatblit (ib 56 356, 1947) Keeney et al. (BullJHH 77 422, 1945) sodium caprylate ointment Peck and Russ (ADS 56 601, 1947) propionate-caprylate mixtures, review and bibliography
Naftalan (Ormsby NEngJM 224:673 1941)
Phenyl Mercuric Compounds (Goldman et al. ADS 47 860 1943)
Propionic Acid Derivatives (Keeney et al: BullJHH 73 479, 1943 75:377 393, 410, 417, 1944)
Sodium Borate (Ingels: CalifWM 54 120 1941 2 per cent soaks or as powder for feet)
Sodium Caprylate (Keeney et al. BullJHH 77 422, 1945 fungistatic ointment)
Streptothricin (Greenbaum J 129:1015 1945 167 units per gram greaseless ointment base for interdigital)
*Sulfonamide (Lewis and Hopper ADS 44:1101, 1941 sulfanilamide best, inhibits T gypseum not C albicans)*
TCAP (trimethyl cetyl ammonium pentachlorphenate) with undecylenic acid is active and effective, according to Foley and Lee (JAmPharmAssn 36:198, 1947)
Tetraiodomethenamine (Sharlit: ADS 40 683, 1939; in collodion, releases iodine slowly).
Undecylenic Acid Derivatives (Shapiro and Rothman ADS 52:166, 1945) Desenex ointment preferable to Sopronol zinc undecylinate enhances fungicidal activity (Sullivan and Fishbel JID 10 291, 1948)
Various Prescriptions (Peck and Schwartz: PHRp.s 58 337 1943)
Zephiran (Hopkins et al. BullUSAMD June, 1944 p. 42.)
Zinc chloride 1/100 molar (1.7 gm. per liter) permanently inhibits respiration of fungi (Nickerson Sc 103 484 1946)

**Treatment of Tinea Corporis.**—The disease as a rule responds to any of the parasiticides, such as Schalek's paste. This may be rubbed in repeatedly until the skin becomes *slightly sore and scaly; then treatment should be stopped for several* days while one waits to see whether more is required.

**Tinea of the Feet and Hands.**—Not a high proportion of what we see called tinea of feet or hand is fungus infection in whole or even in part. Whitfield's ointment is unsuitable for coccic infection, dermatitis dependent on focal infection, contact dermatitis, or dermatophytids, all of which are of frequent incidence. However when tinea is the correct diagnosis, circumstances favoring the organisms may be altered by washing the feet with soap each night, rinsing them well and wiping away scaly accumulations. The toes should be dried carefully after bathing. A dusting powder is then useful. The shoes should be loose particularly at the toe. Vesicles should be opened and painted with 10 per cent aqueous solution of silver nitrate. The feet should be soaked in some antiseptic foot bath such as 1 5,000 potassium permanganate or 1 10,000 bichloride of mercury. The soaks may last 10 minutes, two to six or eight times a day using lukewarm water. In severe cases the patient would be off his feet which between soakings should be elevated, dry and exposed to the air.

In chronic infections with interdigital maceration and scaling about the toes and on the soles, daily washing and dusting are advisable. Silver nitrate is especially useful swabbed over the involved area. Ointments which provoke scaling such as Schalek's paste or half strength Whitfield ointment, may be rubbed in twice a day, the feet being washed once a day with soap and water. Scaling provoked by the medicament must not be mistaken for scaling provoked by infection. The ointment should be used for several days, then omitted for several days. Nails must be examined and treated appropriately. X ray therapy directed at the entire sole for control of hyperhidrosis may be advisable but it will not cure psychosomatic excessive perspiration. Medication of shoes or socks results in more harm than benefit, we believe. Reinfection comes from infected nails or from other persons, and permanent cure *is not* to be promised or indeed even sought. Certainly physicians themselves often carry them of the feet for years neglecting it when it is not bothersome. See also JIn D 3: 523 562, 1940 Caro (YBD 1944, p. 239) Montgomery and Casper (J 123: 77 1943).

In so called fungus infections of the hands, Ayres and Anderson (CalWM 64: 67, 194.) demonstrated organisms in only 1 per cent. Monilia comprised about one fourth of these. Kerio... seen in persons who handle animals. Moniliads... see p. 324.

PREVENTION of pedal dermatomycosis may be accomplished by keeping the feet clean and dry, wiping between the toes after bathing, and using a nonirritant fungicidal such as Desenex powder (Schwartz OccupM 3 543 1947). In the tropics, Jolly (BMJ 1 726 1948) prevented spread of the disease by supplying clean towels, wooden clogs, and a foot powder to each soldier, treating bodily lesions as they were *discovered* with 1 *per cent chrysarobin in Lassar's paste* and interdigital lesions with 1 per cent brilliant green plus 3 per cent salicylic acid in alcohol.

**Onychomycosis** is extremely persistent. Mechanical riddance of the major portion of fungus bearing tissue is an important step. Infected nail material should

be filed or drilled away once a week. Such mechanical débridement must be pursued energetically. Saturated alcoholic solution of silver nitrate, tincture of iodine, or 3 per cent chrysarobin in chloroform is a satisfactory agent to apply to the scraped nails. Ointments are not satisfactory. If fungistasis is secured, the nail will eventually replace itself. While Wigley (BMJ 2: 560, 1943) described the difficult technic of surgical ablation of a nail, Montgomery (J 130: 647, 1945) advised conservatism, using painstaking débridement and strong fungicides.

Onychomycosis due to *T. purpureum*, where little or no involvement of plantar skin appears, was discussed by Montgomery and Casper (NYSJM 46: 2038, 1946). The free edge of the nail is first affected, and yellow streaks extend longitudinally under the plate, enlarge and render the nail yellow, brittle, and dystrophic so that it may detach. They used repeated débridement with an electric drill and applied 40 per cent salicylic acid plasters to be changed weekly, later tincture of iodine or 1 to 3 per cent chrysarobin ointment.

**Tinea of the Crotch and Axilla** commonly depends on the presence of infection elsewhere, particularly of the feet, which must be examined and treated appropriately. Chrysarobin in chloroform is our favorite remedy, but its use must, in "hot" cases, be preceded by a day or two of boric acid compresses. Desenex powder is excellent. The application of 5 per cent silver nitrate and the use of 1:10 000 bichloride of mercury as cool wet poultices, applied for 10 or 15 minutes two to six times a day, generally serve to control the infection. The underwear and trousers must be loose so that the parts are well ventilated. Schalek's paste may be rubbed in, left on overnight and washed off with soap and water the next morning. In women mycotic infection of the crotch is often due to mycotic vulvovaginitis, and 1:5,000 potassium permanganate douches twice a day should supplement external therapy.

**Tinea of the Beard.**—Localized inflammatory mycotic infection, kerion, is treated by the removal of loose hairs, the application of wet packs of 1:10 000 bichloride of mercury and small doses of roentgen therapy. Sulfadiazine by mouth may be helpful. When the infection is disseminated and chronic rather than deeply inflammatory and localized, the problem is more difficult.

**Tinea of the Scalp** is often epidemic among children. Prophylactic measures are essential, and this involves isolation and control of tonsorial sanitation. The hair should be closely clipped, and a snugly fitting paper cap should be worn continually. The scalp should be washed with nonmedicated soap and water once a day or once in two days, depending on its soreness. Infections with *Microsporum audouini* are highly resistant as a rule, but not always (Livingood and Pillsbury, JInD 4: 43, 1941, cured 70 per cent without x-ray); these are only sometimes inflammatory and are likely to require epilation, roentgen or by forceps. *M. lanosum* infection may be treated successfully by showing the mother how to remove all infected hairs with a good forceps, with instructions to shampoo the head daily and to follow drying after the shampoo with a thorough rubbing in of 4 per cent salicylic acid and 6 per cent sulfur in petrolatum. Alternate use of 10 per cent ammoniated mercury and 5 per cent mercurochrome served well for Cleveland (CanadMAJ 36: 32, 1937). MacKee et al. (JInvD 7: 43, 1946) reported a topical method involving trimethyl cetyl ammonium pentachlorphenate, citric and propionic acids, and a detergent vehicle. Salicylanilide 5 per cent or copper undecylenate saturated solution in Carbowax was effective in the Hagerstown, Md., epidemic of 1944-1945, when properly used (Schwartz et al., J 132: 58, 1946).

Roentgen Epilation may be judged safe if performed expertly with reliably calibrated x-ray machines. A these marker is simple and convenient. It consists of a flexible plastic band which fits about the head equatorially and has two bands attached to it which cross the scalp in great circles at right angles to the circumferential band and to each other. The circumferential band is located 5 inches, plus or minus ¼ inch or so, from the vertex intersection of the crossed bands, which are placed on the head in the sagittal and coronal planes. Five points are thus marked by the vertex point and the four points 90 degrees apart on the circumferential band. The point over the middle of the forehead is placed about 1 inch within the hairline, and the nuchal point falls about 1½ inches within the scalp line. The epilating dose of 350 to 400 r at about 100 KVP is delivered with care that the center of the beam is accurately perpendicular to the scalp at each of the five points, nonhairy skin being adequately shielded. The hair loosens and begins to fall on about the seventeenth day. Its regrowth eventually is pretty certain.

During the defluvium, abetted by manual epilation, energetic fungicidal therapy is employed. Buried and broken hairs may be encouraged to come out by a detergent grease such as Carbowax 1,500, Becker (1946) told us. Local rather than whole scalp epilation may be adequate (Lewis and Hopper, ADS 49: 107, 1944). Care is con-

trolled by careful examination in Wood's light. Isolated, stubborn, fluorescent hairs may be removed by electrodesiccation so hastening cure (Costello ADS 54: 10, 1946)

Roentgen epilation may be repeated probably with safety if the interval between the 2 treatments is not less than 3 months, but if a third epilation is given, permanent damage and hair loss are expected (Hazen ADS 56 539 194 )

**Kerion of the Scalp** heals spontaneously Manual epilation helps.

**Trichophyton Purpureum Infection** is sufficiently distinctive to be recognized from its clinical manifestation with some assurance (Lewis et al. ADS 37 822, 1938) The lesions are likely to be solid, lichenoid plaques, spreading at the borders with follicular papules, affecting the regions of the groin, back, thigh, or umbilicus. They are superficial, pruritic and extremely rebellious. Rarely granulomas are produced by this organism. Undermining and destruction of the nail plate are



Fig. 336.—F ic scutula in scalp (Dr George Miller MacKee.)



Figs. 337 and 338.—Tinea imbricata, Fiji cases. (Dr H M. Robinson, Jr )

typical when onychomycosis is the case. Hair involvement is exceptional, lesions being scattered follicular pustules and the organism behaving as an ectothrix. In therapy potent topical agents must be used with persistence; see p. 316.

Extreme distribution and resemblance to dermatitis herpetiformis were reported by Tolmach and Schweig (ADS 41: 733, 1940). Experimental infection of rabbits interested Beiss (ADS 49: 24, 1944). Cultural studies were detailed by Lewis and Hopper (ADS 41: 893, 1940). Swartz and Conant (ADS 43: 614, 1940) preferred the name *T. rubrum*, and recommended inhalations of ethyl iodide in treatment.

Favus is the dermatosis due to infection with *Trichophyton (Achorion) Schoenleini* or any of several closely related organisms. It is characterized clinically by saucer shaped, yellowish scutula. Infection may involve the hair, nails or glabrous skin, or all of these. The scalp is the commonest site. A scutulum tends to enlarge peripherally and neighboring lesions coalesce to form thick, mortarlike masses which possess a peculiar characteristic odor like that of a mouse nest. The hair becomes dull, dry, lusterless, and brittle. In long standing cases the follicles undergo atrophic obliteration, leading to cicatricial alopecia. The disease progresses tediously and it may endure over a period of many years. Favus is distinguished from tinea only by positive identification of the organism. Favids are the analogues of trichophytids.

Etiology.—The disease may be transferred by handling infected animals, but transference from infected human beings is the usual route.

Treatment.—The treatment of favus of the scalp is essentially that of tinea capitis. Roentgen epilation is highly desirable. Parasiticides are those commonly used in tinea (Barrett: ADS 33: 126, 1936; MacKee et al.: NYSJM 41: 1731, 1941).

Tinea Imbricata (Tokelau ringworm) is a dermatomycosis of warm, moist climates, due to various fungi of the genus *Endodermophyton concentricum*. The infection is characterized by the widespread occurrence of scaly patches which often assume a concentric arrangement. The eruption may become universal and be mistaken for ichthyosis. The face, scalp, palms, soles and nails usually escape. The health is unaffected. Chronicity of the disease is notable. It responds only stubbornly even to appropriate treatment, and relapses are common. Castellani fuchsin paint is fairly satisfactory. Chrysarobin ointment may be useful (Castellani: BJD 25: 377, 1913; Gomes: ADS 53: 243, 1946).

## TINEA VERSICOLOR

Tinea versicolor (pityriasis versicolor) is a superficial dermatomycosis due to *Malassezia furfur*. Yellowish or brownish macules are found usually on the chest and shoulders, although various regions including the scalp and even generalized involvement have been seen (Costa and Junqueira: ADS 47: 546, 1943). The patients are generally adult. The disease begins with one or more small, rounded, noninflammatory macules, which enlarge slowly and may reach a diameter of 3 cm. or more, their surfaces being covered with fine scales. Symptoms are almost wanting as a rule.

**Etiology and Pathology.**—*Malassezia furfur* is easily detected in scrapings immersed in 10 per cent KOH. It has been cultivated (Moore: ADS 41: 253, 1940). Persons with moist skins, such as sufferers from tuberculosis, seem especially liable to infection.

**Treatment.**—The disorder is harmless and responds favorably though seldom permanently to medication. The skin may be swabbed with half saturated sodium thiosulfate solution and allowed to dry, then swabbed with 25 per cent vinegar (Dennie), which frees nascent sulfur and sulfurous acid. Three per cent salicylic acid and 5 per cent precipitated sulfur in petrolatum will serve. Five per cent crude coal tar in lanolin and petrolatum is messy but effective. The underwear must be sterilized to guard against reinoculation.

**Tropical Tinea Versicolor.**—Yellow, white and black forms have been described (Castellani: JCutD 26: 393, 1908). The neck and upper part of the chest are most often involved.



Fig. 389.—Tinea versicolor



Fig. 390.—Tinea versicolor after ultra-violet irradiation, showing reddening of skin between opaque patches of dermatomycoses pseudoachromia parasitica (see p. 633)

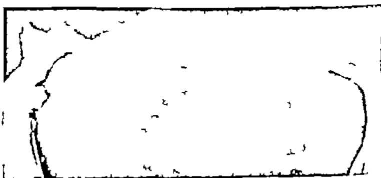


Fig. 391.—Achromia parasitica. (Pardo-Castello, AD&S 25: 788, 1932.)

**Achromia Parasitaria.**—Depigmentation may result from superficial fungus infections of a sort resembling tinea versicolor. There appear dirty whitish spots, slightly inflammatory at first but soon losing this aspect, becoming scaly and eventually becoming quite devoid of scales. After depigmentation has occurred, the lesions resemble those of vitiligo or syphilitic leucoderma (Pardo-Castello: ADS 25: 785, 1932). See Pseudoachromia parasitica, p. 553.

## ERYTHRASMA

*Actinomyces minutissimus* is a delicate fungus with spores and mycelia about 1 micron in diameter. It produces irregular but sharply circumscribed, reddish brown, slowly spreading, finely scaling dry patches of slightly pruriginous, superficial dermatitis, located usually in the axillary, genitocrural or pubic regions, rarely elsewhere. The patches develop and spread slowly and give rise to slight symptoms. Antiparasitics used in treating tinea corporis are suitable, and garments should be sterilized to avoid reinfection.

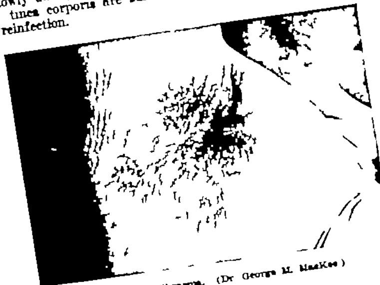


Fig. 192.—Erythrasma. (Dr. George M. MacKee.)

## THE BLASTOMYCOSES

Clinically blastomycoses are chronic infectious diseases due to budding fungi. These commonly attack the skin, giving rise to purplish, moist, papillomatous lesions, and frequently invade internal organs and subcutaneous tissues, giving rise to granulomatous tumors. Histologic features of the mycotic granulomas were reviewed by Moore (JInvD 6: 149, 1945).

Mycologically, Swartz (1947) advised us, blastomycetes are yeastlike fungi which bud both in lesions and in cultures, including *Cryptococcus neoformans* (*Torula histolytica* producing European blastomycosis), *Candida albicans*, and *Pityrosporum ovale* and excluding *Coccidioides immitis*, *Paracoccidioides brasiliensis*, *Blastomyces dermatitidis* and *Histoplasma capsulatum* because while these produce budding in lesions, they grow moldlike on all media at room temperature.

**Blastomycosis of Gilchrist.**—Infection with *Blastomyces dermatitidis* begins as a rule on some exposed surface with a small papulopustule which gradually enlarges. Crusting is present almost from the beginning. The



Fig. 393.



Fig. 394.

Fig. 393.—Blastomycosis of Gilchrist. (Dr Grover Wende.)
Fig. 394.—Blastomycosis of Gilchrist. (Dr John Butler.)



Fig. 395.



Fig. 396.

Fig. 395.—Blastomycosis of Gilchrist. (Dr Ott L. Castle.)
Fig. 396.—Blastomycosis histologic structure showing papillary [illegible] and pseudoepitheliomatous hyperplasia of epidermis. (Dr F. W. Shaw.)

underlying lesion comes to consist of reddish or purplish, irregular papillomatous tumors bathed in seropurulent fluid. The patches tend to extend peripherally and heal in the center with atrophic scarring. Blastomycosis must be distinguished from tuberculosis verrucosa, sporotrichosis, vegetating syphilids, and bromide eruptions. Immunologic aspects were investigated by Peck et al (JImm 38 449 1940) who found 2 polysaccharides which fixed complement of immunized rabbits and provoked tuberculin type reactions on intradermal injection in sensitive individuals, who could be hyposensitized.



Fig. 397



Fig. 398

Fig. 397.—Blastomycosis of groin.
Fig. 398.—Blastomyces in tissue. (Dr F W Shaw.)

Most of the localized infections do not endanger life and respond fairly promptly to appropriate treatment. Scarring usually results. The possibility of systemic dissemination is always present and systemic infections are serious. A young man with forehead lesions, for example, developed meningitis, and autopsy revealed multiple abscesses including several in the central nervous system (Franks and Taylor, ADS 48 88, 1943). Internally iodide has been recommended. Sulfonamides in high concentration inhibit cultures (Noojin and Callaway, ADS 47 620 1943) but they did not benefit a patient of Bayer (Bull USAMD 43 333, 1942) nor did penicillin although huge doses of iodides did. Locally roentgen therapy is especially useful. Tincture of iodine is one of the best parasiticides. Solid carbon dioxide or electrocoagulation may be used. See Gilchrist (BMJ 2 1381 1902), Martin and Smith (AmRevTuberc 39 275 39 488 1939), Smith (J 116 200 1941).

**Coccidioidomycosis.**—Infection with *Coccidioides immitis* apparently is commonly acquired through the respiratory tract. Endemic foci exist in California (San Joaquin Valley), Arizona, Mexico, New Mexico and Texas. The skin test negative on arrival frequently becomes

THE BLASTOMYCOSES After MOORE (ADS 38: 163 1938)

| DISEASE | FUNGUS | CLINICAL CHARACTERISTICS | FUNGUS IN TISSUE OR PUS | CULTURE, GROSS | CULTURE, MICROSCOPIC |
|---|---|---|---|---|---|
| Coccidioidal granuloma | *Coccidioides immitis* | Infectious granuloma, acute, subacute chronic Cutaneous, subcutaneous, or systemic lesion Lesions may be nodular ulcerative, papillomatous, verrucoid, gummatous. | Cells isolated or in giant cells spherical, thick walled, diameter 2-80μ reproduces by endospore formation budding absent. | Colonies flat, somewhat submerged, grayish, becoming white to light cream, with aerial hyphae cottony at times coremioid growth rapid. | Hyphae septate, branching, 0.8–4μ in diameter; arthrosporous cells 2.5–7μ by 5–12μ chlamydospores abundant, 5–8μ in diameter racquet mycelium; terminal hypnospores 5 × 8μ anaerobic endogenous spore formation. |
| North America blastomycosis | *Zymonema dermatitidis* *Zymonema capsulatum* *Zymonema gruetzum* [illegible] *[illegible]* | Infectious condition often granulomatous. Cutaneous or systemic lesions. Cutaneous lesions primary secondary papulo-ulcerative, verrucous or papillomatous, gummatous. | Simple or budding yeastlike cells, thick walled, 5-30μ in diameter usually approximately 7μ. | Colonies at first yeast like, then coremioid, finally profuse and cottony changing from white to cinnamon; radiating ridges and concentric rings of growth Z. capsulatum remains white. | Hyphae septate, branching, 2 4μ in diameter conidia pyriform or round, pedicellate or sessile, 5μ in diameter; racquet mycelium, 5–8 × 3.5μ chlamydospores terminal or lateral 5.5–7.5 × 12–15μ ascogenous cells spherical, 5–13μ. |
| European blastomycosis | *Cryptococcus hominis* *Atelosaccharomyces hominis* | Similar to No. Am blastomycosis but ulcerative in cutaneous form, with abscesses, little inflammation invades cerebrospinal system. | Thick walled, usually encapsulated, simple or budding cells approximately 5-10μ, occasionally larger | Colonies yeasty or pasty smooth, mucoid to moist, subpulvinate color light cream, becoming light tan to brown with age; growth fair | Spherical to ovoid budding, encapsulated cells approximately 2–6μ in diameter rarely larger no mycelium, pseudomycelium or spores. |
| South American blastomycosis Paracoccidioidal granuloma A. Generalized B. Localized affecting buccal mucosa | (a) *Paracoccidioides brasiliensis* (b) *Paracoccidioides tenuis* (c) *Paracoccidioides cerebriformis* | A Generalized or localized, cutaneous or systemic, granulomatous, papular verrucous or ulcerative acute to chronic usually lymphangitis in spread. B. Lesions localized on buccal mucosa acute chronic verrucous, papillomatous ulcerative, granulomatous lymphangitic spread only in terminal stages. | (a) and (b) Cells spherical or ovoid, 1-30μ in diameter thick wall simple multiple budding of minute, spherical, ovoid or bacillary gemmules. (c) Cell spherical or ovoid, 1-30 in diameter larger than those of P. brasiliensis or P. tenuis; thick walled, with simple or multiple budding of small, spherical, ovoid or elongated gemmules. | (a) White, adherent to substratum and somewhat hard, well-defined, somewhat cottony (b) Mycelium mostly submerged colonies compact, verrucoid or vermiculate at inoculation, showing folds or radiating ridges white; growth slow (c) On agar cerebriform to crinkulate, yeast like, creamy buff, becoming light cinnamon-buff with age; easily separated from substratum, but filamentous, flat and adherent to dry portions of substratum growth slow | (a) Hyphae septate, branching, 1.5–3.5μ, hyphal swellings 3–5μ, spherical, terminal chlamydospores to 15μ conidia lateral, sessile or pedicellate, 3–7μ. (b) Same as P. brasiliensis corresponding structures smaller (c) Hyphae irregular septate, branching, 2 [illegible] with many swellings [illegible] arthrosporous, [illegible]idioid, [illegible] mbell-shaped; chlamydospores spherical, clavate, pyriform or sclerotic, intercalary, lateral or terminal, up to 15μ. |

positive in personnel introduced into such regions (Lee CalWM 61 133 1944) although such primary infection may be asymptomatic or manifested only by what would pass for mild influenza. Such manifestations are often accompanied by erythema nodosum from which most patients recover without complication (Dickson AmRevTuberc 38 711, 1938) Of 1,351 infections reviewed by Smith et al. (AmJPubH 36 1394 1946) 60



Fig. 399.—Coccidioidal granuloma. (Dr Wm Allen Pusey)



Fig. 400

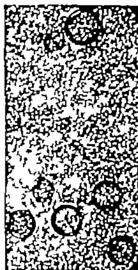


Fig 401.

Fig. 400.—Coccidioidal granuloma. (Dr Grover Wende.)
Fig. 401.—*Coccidioides immitis* in pus. (Dr Fred Weidman.)

per cent were without symptoms and only 25 per cent were clinically manifest. Erythema nodosum occurred in 4.6 per cent and dissemination in only 0.25 per cent, mostly affecting Negro males. Progressive disease is analogous to the overwhelming tuberculosis of childhood. Features of pulmonary x rays range from a small nodular opacity through exudative but clearing lesions to nodular densities which may calcify eventually (Winn and Johnson AnnIntM 17 407 1942). Primary cutaneous infection occurs. While most infected persons recover, some suffer progressive disease. Acute disseminating primary coccidioidomycosis is almost always fatal in from 1 to 6 months. Chronic disseminating disease, coccidioidal granuloma, has a mortality of about 50 per cent. Generalization may follow skin or pulmonic primary disease, presumably via the blood stream.



Fig. 402.



Fig. 403.

Fig. 402.—Chromoblastomycosis. (Dr. J. W. Perkins.)
Fig. 403.—Chromoblastomycosis. (Dr. V. Pardo-Costello.)

In ch[romoblastomycosis] ... gran[u]loma the lesions are found preferentially located on the head, [n]eck, shoulters, [a]nd [u]pper extremities. They are [v]errucose and papillomatous. Th[ey] ... [involv]e mainly the [s]kin and occasionally th[e] mucosae. ... [Cau]liform ra[c]hes h[ave] [b]een noted (Goldstein and McDonald J 121 837 1941). Fever is usual and several ... [i]mprovement follows. The organisms are easily demonstrated.

In chronic co[ccidioida]l gra[nu]loma typically affected are the sternoclavicular joint, the neck, the ... [so]les of the feet and the inguinal regions. The lesions are furunculoid gran[u]lomatous ... lesions. The connective tissues [o]f deep structures are mainly involved and th[e] mucosae are affected only rarely. Th[e] course is slow with remission and relapses. Fever [is] low [or] absent. The [vi]scera are involved t[o] a lesser extent, the organisms are more [d]ifficult to demonstrate and the outlook is better than

in the miliary type of case. Arthritic involvement or symptoms suggesting Pott's disease, appendicitis, or pneumonia may confuse the diagnosis (Rosenberg et al. AIntM 69 238 1942; Quill and Burch AmSurg 120: 670 1944)

The structure of coccidioidal granuloma is that of the infectious granulomas, the causative organisms being found generally within the giant cells of the exudate. They multiply by endogenous formation of spores. In the pus they are doubly contoured spheres 5 to 60 microns in diameter with granular protoplasm. In isotonic saline, sealed under a coverglass, they quickly germinate a septate mycelium (Wilson ADS 57: 561 1948) They grow on dextrose agar The organism has been found in the soil at the place where infection occurred (Davis et al.: J 118: 1182, 1942) Dust control by grading paving and application of oil has reduced the rate of infection (Smith et al.: J 132: 833 1946)

Treatment with potassium iodide has little effect on the course of the disease Antimony and potassium tartrate and roentgen therapy have been used with benefit. Coccidioidin, a vaccinal preparation, has value (Jacobson ADS 40 521 1939 57 561 1948) Doses must be of proper size and timing to immunize Incision and drainage should not be performed. Thymol in doses as great as 6 gm. daily may help (Sox and Dickson: J 106 777 1936) Penicillin is ineffectual.




Figs 404 and 405 — Chromomycosis. Section showing acanthosis, dermal infiltration, and giant cells. Higher magnification reveal thick-walled, brown cells of *Phialophora verrucosa* in the giant cells. (Moore et al J 122 1237 1943.)

**Paracoccidioidal Granuloma.**—South American blastomycosis is a chronic granulomatous disease caused by *Blastomyces brasiliensis*, affecting skin, mucosae, lymph nodes, and viscera (Conant et al. Manual of Clinical Mycology Saunders, 1944) Localized, lymphangitic disseminated and mixed types of cases are described. The generalized disease may be acute or chronic. The fungus may enter the buccal tissues, forming a hard infiltration of the gums, spreading to the lips, nose and margin of the tongue. Affecting the skin primarily lesions may develop upon an abrasion where the fungi have become lodged. Diagnosis depends on identification of the causative fungus (Jordan and Weidman ADS 33: 31 1936)

Chromoblastomycosis is a polymorphous parasitic dermatosis, caused by *Hormodendrum pedrosoi*, *H compactum*, or *Phialophora verrucosa*, productive of a

primarily papular nodular or verrucose painless eruption which may progress with ulceration vegetation, and hyperkeratosis. Verrucosities may be isolated or confluent, and may invade the whole foot or leg or other parts of the body. Infection seems significantly often to follow injury with some form of wood and usually affects an exposed part unilaterally (Weldman and Rosenthal ADS 43 62, 1941). Surgical destruction of lesions, iodides by mouth and intravenously and $CuSO_4$ iontophoresis are recommended by Conant et al. (Manual of Clinical Mycology Saunders, 1944). See Moore (ADS 38: 163, 1938) Smith (J 116: 200 1941) Pardo Castello et al. (ADS 45: 19 1942) Calero (ADS 54 263 1946)

## MONILIASIS

*Monilia albicans* (Zopf 1890) is the type species of the genus *Mycotorula* (Will, 1916) as given by Brumpt. *Candida albicans* is the official name. This fungus causes many different clinical manifestations, which may be localized or widespread and acute or chronic, affecting the skin, its appendages, mucous membranes, and gastrointestinal tract. It is a potent sensitizer provoking eczematous sensitization as well as passively transferable antibodies.

**Clinical Forms of Moniliasis** (Lewis and Hopper NYSJM 38 859 1938) are as follows

| Localized | Generalized | Systemic |
|---|---|---|
| Onychia, paronychia<br>Intertrigo (axillary submammary, inguinal)<br>Erosio interdigitalis (variety of intertrigo)<br>Perleche<br>Superficial glossitis<br>Stomatitis (thrush)<br>Dermatitis, localized<br>Vulvovaginitis | 1 Widespread eruptions usually associated with some of the localized forms. Characteristic flat pustules may usually be observed in some part of the eruption. These pustules become dry and macerated scales form on the surface. With exfoliation, a bright red, moist surface is left with overhanging edges.<br>2. Moniliids. Pompholyx is often monilial. | This group includes cases of pulmonary involvement and massive gastrointestinal infection. Such infections are often associated with cutaneous infection and have proved incurable. |

**Monilial Onychomycosis.**—See p 309

**Monilial Paronychia.**—See p 310

**Monilial Intertrigo**.—Intertrigo is a clinical name applied to any superficial dermatitis characterized by redness, abrasion and maceration, occurring on opposing surfaces. Hyperhidrosis is followed by fermentation and the skin becomes abraded and raw. The gluteal and crurocrotal folds, the inframammary region and the folds of the neck are common locations. Hot weather obesity and binding garments are predisposing factors. Monilia are the organisms usually to blame, although streptococci or staphylococci may be the infecting agents. Cleanliness and dryness are preventive achieved by loose clothing good ventilation and the use of bland dusting powder. Exertion in hot moist weather leads to trouble particularly in fleshy persons. Infections elsewhere as sources of reinfection must be controlled. Vaginal douches using 1:5 000 potassium permanganate and vaginal swabbings with 1 or 2 per cent aqueous solution of gentian violet will control mycotic vulvovaginitis. Wet packs are excellent, using cool 1 500 aluminum acetate in water or 1 10 000 bichloride of mercury. The parts should be dried and dusted generously with borated talc. Ointments meet with little success. Diabetes, if present must be recognized and managed



Fig. 406.—Monilial onychomycosis. (Dr. W. Herbert Brown.)



Fig. 407.—Monilial intertrigo.



Fig. 408.—Monilial vulvitis in an infant.

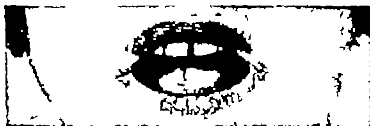


Fig. 409.—Perlèche. (Dr. D. W. Montgomery.)



Fig. 410.—Monilial interdigital dermatitis in laundress. (Dr. James H. Mitchell.)

**Monilial Stomatitis.**—Oral lesions due to *C albicans* are thrush, glossitis and some cases of perlèche

THRUSH is manifest as superficial adherent deposits resembling coagulated milk. The lesions bleed if the membrane is forcibly removed. Circumoral skin may be involved. The disease affects infants and sometimes adults, particularly pellagrins. Epidemics may occur the organism being transferred by unclean utensils. The parasite is easy to find in scrapings Moniliasis of the newborn is related to vulvovaginitis of the mother (Carter et al. AmJOG 39 213, 1940 Waters and Cartwright J 113 30 1939)

GLOSSITIS associated with *Monilia* occurs in sprue and pellagra. Hyperemia of the fungiform papillae and aphthous ulcers occur along with increased sensitiveness to hot fluids, spices, and tobacco smoke There follows atrophy of the papillae so that the tongue becomes smooth and red. An important relationship certainly exists between dietary deficiency and susceptibility to infection. The stomatitis of primary anemia and pellagra responds promptly to appropriate dietary and vitamin therapy

PERLÈCHE is an intertriginous inflammation of the labial commissures A symptom not a diagnosis, perlèche is sometimes due to monilia, streptococci, contactants (soap dentifrice, mouthwash cosmetics) foci of infection or avitaminosis and sometimes one fails to find the cause It is usually bilateral The mucosa is thickened and somewhat macerated. The lesions extend a short distance onto the skin and onto the mucous membranes. In severe cases there are deep wrinkles and sore fissures. The lesions must be distinguished from the mucous patches and split papules of syphilis. When secondary syphilis affects the mouth there are always concomitant signs of widespread syphilitic disease. Perlèche seems to be transferable It has occurred in many individuals in one community such as an orphanage Sebrell (PHRpts 53 2282 1938) showed that women on a diet lacking riboflavine developed perlèche-like lesions The disease is treated by the use of mild astringent mouthwashes, and attention should be given to the diet which must be adequate in vitamin B content Monilial stomatitis is responsive to 2 per cent aqueous solution of gentian violet a nontoxic but unsightly dye which may be used safely

**Monilial Interdigital Dermatitis** (erosio interdigitalis) usually appears on the web between the middle and ring fingers. Women, especially laundresses, are susceptible to the disorder The lesions are superficial inflammatory sharply defined with undermined macerated borders, beneath which monilia can be found Extension over the dorsum of the hand and up the forearm is not rare Such cases are resistant to treatment but dryness, débridement and repeated applications of gentian violet or chrysarobin 3 per cent in chloroform or Castellani s paint (Seale and Clark BMJ 41 927 1948) will usually succeed Diagnosis is easily made by KOH preparations or cultures

**Monilia Pudendal and Perianal Infection.**—Pruritus ani and pruritus vulvae are often due to *Candida* or other fungi such as *Epidermophyton* and the infection is likely to be complicated by medicinal and traumatic irritation Diabetes promotes pruritus because dextrin encourages the growth of mycotic organisms Monilial vaginitis is a common cause of pruritus even in women who do not have diabetes. Monilial infestation of the vagina is commonplace and frequently asymptomatic It occurs in children, virgins, and senile women as well as parous ones. The disease

may be chronic, with exacerbations at times over a period of months or years. Menstruation has the same temporary beneficial effect on the course of the infection as delivery does in cases associated with pregnancy suggesting that estrogen deficiency may be a significant factor. Infantile oral thrush may result from infection in the birth canal (Hesseltine AmJOG 40 641 1940 Minnich JMAGa 30 386 1941 treatment)

**Monilial Vulvovaginitis.**—These types occur (J 110 1733 1938)

1. Creamy vaginitis resembling oral thrush, with painful and reddened mucosa.
2. Creamy vulvitis with intertrigo, which characteristically consists of small, grouped shallow vesicopustules.
3. Ulcerative vulviti severe, with pain, lymphangitis and inguinal adenitis, possibly with mycotic infection of the bladder
4. Eczematoid vulvitis with a vesiculopustular eruption consisting of small punctiform erosions, resembling intertrigo.
5. Mycotic pruritus of the vulva, with few erosions, perhaps, and little discharge diagnosable only by smear and culture
6. Vesiculopustular cutaneous form manifesting disseminated involvement principally of external teguments.
7. Cutaneous intertriginous eczematous form, which is intertrigo-like with without demonstrable organisms i the genitocrural plica, the inflammation prevailing t the pubis, anal region, and medial surfaces of the thighs, with but little visible involvement of the vulva.
8. Inconspicuous vaginiti with disseminated cutaneous involvement in the form of patches of intertriginous dermatitis not amenable t treatment until vaginal infestation is controlled.
9. Moniliids, often consisting f pompholyx-like patches of tiny deep-seated vesicles, which may absorb and result in superficial scaling or which may constitute an inflamed and oozing eczematous dermatitis.

Analogous forms occur in the male involving the inguinal pudendal and perianal regions. Pruritus ani may in some instances be cured by oidiomycin hyposensitization (Fowle et al JInvD 3 193 1940)

Diagnosis of Monilial Vulvovaginitis.—The exudat is acidic. Smears show budding yeasts. Mycelia ppear in the smears at t mes of ma imum severity of clinical symptoms.

**Infantile Dermatomycosis** is usually monilial. In these cases of infantile eczema, i wh h there occu deep red circular and o al, circumscribed but coalescing patches f oozi g, rt h de m titis, the infection i l kely to be monilial and it may ha riginated th b rth canal. Response i fa orabl to 1 per cent aqueous solution of gentia olet

**Monilial Meningitis** has been known to occur though it is rare. Pressure of the spinal fluid is high giving rise to headache and edema of the optic nerve head. Diagnosis depends on demonstration of the organism in the spinal fluid. The patient of Zimmerman et al (J 135 145 1947) who also had oral thrush, recovered, probably as the result of the administration of streptomycin

**Monilial Systemic and Generalized Cutaneous Infections** are comparatively rare. The face, ears, neck, upper chest and mouth are usually involved, and thick, dry brownish crusts occur on the skin. The majority of such cases, complicated by chronic monilial pneumonitis and gastroenteritis, eventuate fatally. At no time is severe inflammatory reaction present. The condition i afebrile. No known form of treatment cures, although a patient of Sulzberger (ADS 40 834 1939) was helped by sulfapyridine. See Tulipan and Mu katblit (ADS 46 642 1942)

**Immunology Skin Tests and Vaccinal Therapy in Moniliasis.**—The humoral and tissue reactions to oidiomycin are analogous with those to trichophytin. *Candida* is a potent sensitizer but treatment by vaccinal hyposensitization is seldom helpful.

**Moniliids** are allergic eruptions analogous to trichophytids. As a rule they consist of tiny closely aggregated, intra-epidermal vesicles, and they may be set upon a more or less inflamed base, located on the hands, legs or flexures. They may depend on foci in the nails, glabrous skin, tonsils, mouth, vagina auditory canal lungs or gut

**Etiology.**—Infection with monilia, like all infections, depends both upon the soil and the organism. In food deficiencies, particularly avitaminosis B and in diabetes the individual is more vulnerable. See p 299.

**Treatment.**—To be comprehensive and permanently effective, treatment must be directed at the eradication of all foci, both in the skin and elsewhere Unfortunately therapy directed at the gastrointestinal tract does not succeed. The accessible parasitized tissues should be kept dry and ointments have little to commend them. Gentian violet and chrysarobin are among the effective parasiticides. Baths in 1 8 000 bichloride of mercury are useful. Douches of 1 5 000 potassium permanganate are fairly satisfactory and, in pregnancy suppositories of 1 1 000 merthiolate are fairly satisfactory (McIlrath M J Austral 2 54, 1946) Cool, moist packs for 15 to 30 minutes, alternated with drying in a current of air under the influence of radiant heat, are effective. Roentgen therapy offers temporary alleviation of inflammation but it must not be repeated beyond the limit of tolerance In stomatitis, cleanliness is an important prophylactic measure Fingers should not be put into babies mouths. Sodium perborate may be used for both tooth powder and mouthwash. Vitamin B complex should be given in adequate dosage. See Bechet (NYSJM 43 2065 1943)

## SEBORRHEIC DERMATITIS

**Symptoms.**—The common form, dandruff, affects the scalp, and is characterized by diffuse scaliness, the scales being greasy and yellowish. The disease appears to be due to *Pityrosporum ovale* (Kile and Engman ADS 37 616 1938) and so is described with the mycoses. Discussion of the etiologic relationship of *P ovale* to seborrheic dermatitis, admittedly dubious, is given by Lewis and Hopper (Introduction to Medical Mycology Year Book Publishers, 1943)

The lesions may be dry with grayish branny scales, or they may be oozing and crusted, constituting the eczema capitis of older writers. Superinfection accounts for the weeping however it is thought and streptococci, staphylococci and contactants commonly complicate seborrheic dermatitis. From the scalp the disease often spreads to the forehead, brows, nose and cheeks, so constituting the dry skin of cosmeticians. Psoriasiform patches may occur in the axillae over the sternum, about the umbilicus, and in the crural folds The margins of the eyelids are involved in many cases. Alopecia probably does not result from dandruff Streptococci may produce scaling intertrigo and postauricular fissuring, distinguished only with difficulty from seborrheic dermatitis. Acne vulgaris is usually complicated by pityriasis of the scalp and face. This is probably due to the fact that *Pityrosporum ovale* finds the oily skin of the



Fig. 411.—Seborrheic dermatitis of scalp and ear



Fig. 412.—Seborrheic dermatitis, neck.



Fig. 413.—Seborrheic dermatitis, axilla.

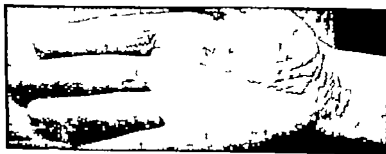


Fig. 414.—Seborrheic dermatitis, palm.

acne patient a ground where it can luxuriate (Benham JInvD * 187 1939 Emmons PHRpts 55 1306 1940)

**Etiology**—Excess of oily food, particularly milk, cream butter chocolate and cod liver oil is a predisposing factor and hypothyroidism is also We think the disease must be parasitic, for it is transmitted, yet *Pityrosporum ovale* may be as profuse in apparently normal scalps as in cases of severe dandruff (MacKee et al. JInvD 2 31 1939)

**Treatment.**—It may be advisable to put the patient on a low fat diet and to adjust a dosage of thyroid Vitamin B complex is often recom-

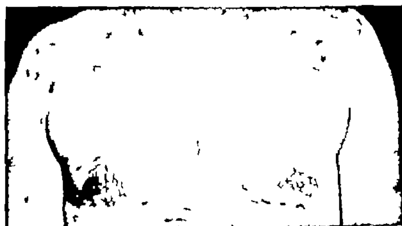


Fig 415.—Seborrheic dermatitis, psoriasiform (Dr F Ronchese.)

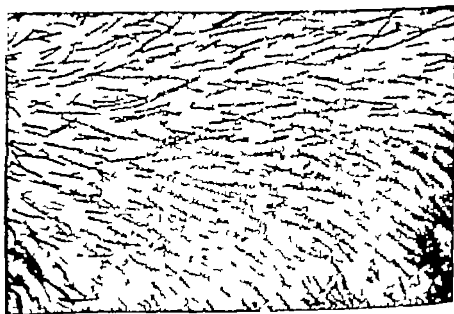
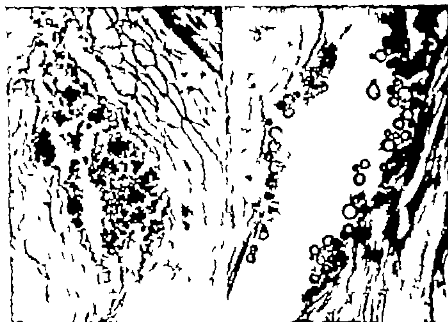


Fig. 416.—Sebor[illegible] dermatitis of scalp dandruff (Dr Merrl Moore)

mended See Wise and Sulzberger (YBD 1941 p 7) For the scalp a valuable prescription is

| | | |
|---|---|---|
| ℞ | Phenol | 1 0 |
| | Mercuric chloride | 0 1 |
| | Resorcinol* | 8,0 |
| | Alcohol (70%) | to 180,0 |

Sig Rub into scalp several nights a week as directed particularly after each shampooing Shampoo every 10 to 14 days. Use no brush because it cannot be sterilized satisfactorily Use a cheap new comb after each shampoo to avoid reinfection. Shampoo at home after each haircut.



Figs. 417 and 418.—Pityrosporum ovale in section of scalp high magnification. (Dr Morris Moore )

A salve works better in thick, severe cases 4 per cent salicylic acid and 6 per cent precipitated sulfur in a water-soluble base such as Carbowax, or 5 per cent ammoniated mercury

Dermatitis venenata particularly if it involves the neck or face is readily complicated by seborrheic dermatitis. The combination resembles so-called lichenified eczema It may be cured by first allowing the moiety of the dermatitis which is due to chemical irritation to heal by using bland applications and avoiding all irritating contacts then by using 2 per cent crude coal tar on remaining parasitic irritation

## SPOROTRICHOSIS

**Symptoms.**—Sporotrichosis is contracted generally by those who come in contact with the soil and shrubs, and infection follows some trifling

* Duresol, a proprietary resorcinol monoacetate may be substituted.

**Prognosis and Treatment.**—Localized cases have a favorable outlook, systemic and disseminated infections less favorable. Systemic involvement consequent to local disease is always possible. Iodides have long been standard therapy but sulfonamides soon proved their worth when they became available (Dobson et al., J 116: 272, 1941). Penicillin is also often effective (Muskatblit, ADS 56: 706, 1947), generous doses being advisable. The patient of McCrea et al. (JLCM 30: 509, 1945) responded to 120,000 units every 3 hours after failing to respond to 20,000. Of 11 cervicofacial cases 7 were cured and 4 arrested by Dobson and Cutting (J 128: 856, 1945) using penicillin or sulfonamide, one being sometimes more effective than the other. Locally, surgical drainage and roentgen therapy should be employed. Thymol, 10 to 20 per cent in olive oil, may be applied locally and injected into the sinuses, and 1 to 2 gm. of thymol in capsules may be given by mouth daily on an empty stomach (Myers, J 108: 1875, 1937). In a study of 16 cervicofacial cases, Lamb et al. (J 134: 351, 1947) concluded that roentgen therapy and sulfadiazine by mouth suffice in uncomplicated instances, while penicillin must sometimes be given in large dosage over a long period of time and is valuable. If osteomyelitis of the jaw occurs, orthopedic or even plastic surgery may be necessary. Penicillin in 45 cases gave best results in pulmonary, abdominal, and pelvic infections, reported Nichols and Herrell (JLabClM 32: 1405, 1947). Sulfonamide and penicillin cured one patient with central nervous system involvement (Jacobson and Cloward, J 137: 769, 1948).

## MYCETOMA

Mycetomas are granulomatous mycotic lesions enclosing fungus grains of various species, shapes, and colors. The grains are formed by felted mycelium, and they are discharged through more or less extensive fistulas. In contrast with the tineas which in general produce only superficial disease, the mycetomas are due to other fungi which produce deeply seated granulomatous inflammation. They gain access into the human body through injuries as a rule and the foot is particularly



Fig. 423.

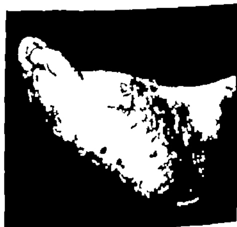


Fig. 424.

Fig. 423.—Madura foot. Texas case. (Dr. O. Garcia.)
Fig. 424.—Mycetoma. (Sutton, R. L., Sr., J 60: 1230, 1913.)

vulnerable Madura foot is a clinical entity characterized by swelling and gradual disintegration of the subcutaneous structures and the formation of sinuses. Fungus granules are found in the exudation from these. They are composed of voluminous, septate mycelial filaments possessing definite cross walls and forming chlamyd spores. Maduromycoses have been classed according to the bl kish whitish or reddish colo of th fungu grains, but grains of the same color may be produced by more than one parasite. There have been identified a causative organisms species of Nocardia, Allescheria, Aspergillus, Penicillium, Madurella, Indiella, Cephalosporium, Monosporium, and Glenospora (Conant et al.: *Manual of Clinical Mycology*, Saunders, 1945, modifying Gammel ADS 13 241 1927); Burns et al.: AmJClPath 15: 85 1943). The earliest lesion may be a papule, deeply seated nodule or abscess which ruptures and becomes fistulous. Tedious progress ensues, with deformity invasion of tendon, muscle and bone, nd the development of induration, nodules, and multiple fistulas. *Secondary infection may cause death.* Treatment is likely to entail eventual amputation but sulfonamides (Dixon: NavMMonth 68: 281, 1941) and penicillin offer hope. Pe icillin failed in 1 of the 2 patients of Twining et al. (BullUSAMD 46 417 1946)

## HISTOPLASMOSIS

Histoplasmosis, caused by *Histoplasma capsulatum*, is an infection characterized by irregular pyrexia, hypochromic anemia, emaciation, and enlargement of the liver spleen and lymph nodes (Conant et al Manual of Clinical Mycology Saunders, 1945). Ulceration of the oral mucosa, especially the tongue and of the pharynx and larynx occur frequently (Parson and Zarafonetis AIntM 75 1 1945). Darling, who originally described the disease (J 46 1283, 1906) noted its resemblance t kala azar Lymph node invol ement may simulate Hodgkin s disease. Bone marrow involvement accounts for the anemia. Diagnosis is accomplished by identification of the organisms in biopsies, but the skin test probably pec fi (Peruzzi et al. J 117 436 1941). The frequency of asymptomatic positive reactors suggests that many an infection, like coccidioidomycosis subclinical.

Of the 1 actual and 3 possible ca es of cutaneous histoplasmosis collated by Curtis and Grekin (J 134 1 17 194 ) 13 had granulomatous or ulcerative lesions,



Figs. 423-4 7.—Histopl smosi. The same tongue in January 1944, and 4 months lat nd the h lo in section (Dr F M. Keddie.)

3 showed nodular lesions, 3 had papulonecrotic lesions, and had abscesses. In 10 cases the cutaneous lesions were distributed over the face and neck, and in 6 of these they were adjacent to the orifices. Lesions were present on the trunk in 4 cases, the extremities in 4 the male genitalia in 2 and generalized in 1 Of 19 cases of histoplasmosis of mucosae adjacent to the skin, 7 were granulomatous and 16 were ulcerative, usually very painful. Nodules ranging from several millimeters to walnut size were described in 5 cases, hemorrhagic patches or crusts of various sizes were noted in 4 cases, fissures in 2 and perforation of the nasal septum in 3. Lesions were present in the nose in 4 instances, on the tongue in 7 on the buccal and labial mucosae in 5, on the palate in 5 gingival in 3 and hypopharyngeal in 7

In a classic review of 88 cases Miller et al. (ADS 56 15 1947) noted that the lesions of histoplasmosis may resemble those of tuberculosis, syphilis, the deep mycoses or lymphoblastoma, and that the systemic disease must be distinguished from kala azar malaria, dysentery and cancer The cytologically nonspecific chronic infectious granulomas contain macrophages as their basic reacting cells, and this inflammation may produce ulcers and gummas of the mouth, papules, plaques and punched out ulcers, purpuric lesions, abscesses, and furunculoid or impetiginoid lesions, localized or generalized.

Treatment is unsatisfactory If the disease is identified, death may be expected within 6 months.

## RHINOSPORIDIOSIS

Rhinosporidiosis is manifested clinically by pedunculated or sessile raspberry like, polypoid friable tumors consisting of tightly packed granulomatous tendrils or lobules, in the fimbriae of which are white fungus spherules which resemble bags of myxoid matter Lesions occur on the conjunctiva pharyngeal, nasal, and genital



Fig. 428 —Rhinosporidiosis mucosal l sations and cutaneous implant in Indian (Allen nd De IndMGaz 77 376 1936)

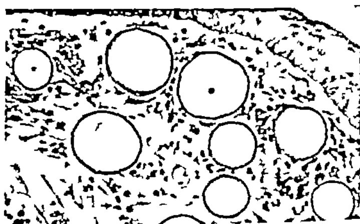


Fig. 429 —Rhinosporidiosis section showing cystic parasit s. (Dr Edw A. Gall)

mucosa, and skin. Cutaneous lesions, solitary or multiple, usually are secondary to mucosal foci, according to Allen and Dave (IndMGaz 71 376, 1936 60 cases, bibliography) Reviews are given by Ashworth (Trans. Roy Soc. Edin. 53: 301, 1923) and Karunaratne (JPathBact 42: 193, 1936, color plates) Ocular cases were collated by Kaye (BJOphth 22: 449 1938); he likened the typical lesion to a cockscomb and described the villous polypi with easily bleeding granulations the crypts of thickened epithelium, the granulomatous inflammation with plasma cells and lymphocytes, and the rhinosporidium cysts, chiefly subepithelial, their white sporangia macroscopically visible on the surface of the lesion. The organism has not been cultivated. The in fection remains local but is unsightly uncomfortable, and sometimes obstructive to air passages. Cure may be sought with surgery Neostibosan seemed adjunctively helpful t Allen and Dave. Most cases have occurred in India and South Africa, but of the 13 reported by 1942 in the United States, 4 were Texan (Pasternack: TexasSJM 38: 285, 1942)

## TORULOSIS

Torula Histolytica (Cryptococcus Neoformans) is a yeastlik fungus found in tissue, spinal fluid or pus as a singl budding spheroid 5 to 10 microns in diameter surrounded by a wide refractile and characteristic gelatinous capsule (Swartz Med cal Mycology 1943) Acneform, furuncul id, and gummatous lesions of th skin as well as deep nodules and abscesses may be caused by it, but pulmonary and especially neurologic lesions are more significant and consequential. Central nervous system ryptococcosis diagnosed by finding the fungus in the spinal fluid, is regularly fatal within 6 months. (Mook and Moore ADS 33: 951 1936 Conant et al.: Manual of Clinical Mycology 1943.)

## RARE MYCOSES

**Geotrichosis**, producti e of chro ic bronchitis with gelatinous sputum or pul monic disease simulating tuberculosis, may affect the oral mucosa in white patches distinguished from thrush simply by direct examination of scrapings, which reveal characteristic rectangular spores.

**Aspergillosis** may induce granulomatous and exudati e lesions of the kin and external ear as well as pulmonary, osseous, and meningeal involvement There is always doubt f the pathogenicity of aspergilli.

**Penicillia** have been cultures from cases of otomycosis.

**Mucormycosis** has been diagnosed in paronychia f orange workers (Sutherland Campbell and Plunkett: ADS 30 651 1934) otomycosis, and furunculoid lesions of the face (Wade and Matthews J 114: 410 1940)

*Clinical Parasitology* by Craig and Faust (Lea & Febiger 1945) is our principal authority in this chapter Brumpt's *Précis de Parasitologie* (Masson et Cie 1936) and Riley and Johannsen's *Medical Entomology* (McGraw Hill) are also followed Stitt and Strong's *Tropical Diseases* (Blakiston 1942) and Ash and Spitz's *Pathology of Tropical Diseases* (Saunders, 1945) are valuable as well

## PROTOZOA

### AMEBIASIS

Endamoeba histolytica is a rhizopod protozoon manifesting trophozoite, precystic, cystic, and metacystic stages in its life cycle. In unstained preparations the trophozoites range from 15 to 60 microns in diameter, averaging about 20 microns. The ectoplasm is glassy clear, the endoplasm finely granular and the nucleus almost invisible. Ectoplasmic pseudopodia are rapidly and actively extruded in freshly passed stools, but motility is sluggish in cool preparations. The habitat is the distal gut and transmission is accomplished by ingestion of substances, usually a polluted water supply contaminated with feces containing cysts of the parasite. Asymptomatic carriers exist.



Fig. 430 Fig. 431. Fig. 432.

Fig. 430—Amebiasis, perianal lesion in a Chinese with amebic colitis. (Ngai and Frazier ChinMJ 47 1164 1933.) See Fig 431

Fig. 431.—Perianal amebiasis cured by routine treatment of colitis with emetine

Fig 432 —Ameba in region of dermoepidermal junction, provoking acute purulent inflammation (Drs. Ngai and Frazier )

**Symptoms.**—Cutaneous involvement may be classified as occurring by extension by inoculation and from allergy (Touraine and Duperrat Presse méd 47 1086 1939) Extending in the skin following surgical attack upon an amebic visceral abscess, amebic dermatitis is ulcerative starting within one to three weeks as a rule with a little redness and developing black necrosis or furuncular anthraxlike lesions. Perianal extension of colonic and rectal disease occurs. Inoculation with purely cutaneous amebiasis is rare the lesions being extensive ulcers or sometimes

circumscribed torpid abscesses which crust, extend peripherally and heal with scarring Genitalia of male or female may be inoculated. Allergic dermatoses dependent on amebiasis include anal pruritus, urticaria rosacea-like disease, buccal melanosis, and desquamative erythema from emetine or other medicines. Amebic ulcers generally are large, circular ragged, purulent lesions, with deep red undermined, swollen edges. Recently reported interesting cases include those of Jermstad and Launy (Texas SJM 37 713 1942) Hermann and Berman (J 120 827 1942) and Cleland (JTropM 47 54 1944) Diagnosis requires positive identification of the organism.

Treatment with emetine a hazardously toxic alkaloid from ipecac is usually successful, the hydrochloride being given in 0 065 gm. (gr i) doses subcutaneously for not more than 12 doses in a course Chiniofon (Yatren), Diodoquin, Vioform and carbarsone are also effective (see Craig and Faust)

## TRICHOMONAS VAGINITIS

The class Mastigophora, flagellate protozoa, includes the Trichomonadidae of which *T vaginalis* is associated with mucosal disease of dermatologic interest. The organism is pear-shaped, about 10 microns long and possessed of 3 to 5 anterior flagella. The marginal filament along the undulating membrane is not prolonged into a free flagellum, and there is a well-defined parabasal body Pathogenicity has not been positively demonstrated.

**Symptoms**—While many women harbor the organisms, comparatively few complain Vulvar pruritus is sometimes attributed to them. Redness, excoriation, edema, pinpoint vesicles and minute caruncle-like lesions were described by Hollander (ADS 36 142, 1937) Kessel and Gafford (AmJOG 39 1005 1940) recorded histologic changes, finding trichomonads in acute inflammation with focal necroses their implants of exudate into normal vaginas produced the disease but implants of cultures did not. Leucorrhea may be profuse. It is grayish-white seropurulent and peculiarly foamy when the speculum is introduced. Symptoms tend to be cyclic the exacerbations overlapping the period of menstrual flow The organisms are readily demonstrated on microscopic examination of a hanging droplet of saline to which exudate has been added.

**Treatment.**—Insufflation of the vagina twice a week is effective, using a powder containing acetarsone 12 parts, salicylic acid 2 and sodium bicarbonate and kaolin in equal amounts to make 100 The vaginal pH should be kept less than 5 by means of lactic acid douches, a dram to the quart of water which should be used twice a day between periods and three times a day during the menses. Hugh Hamilton advises See Karnaky (AmJSurg 48 217 1940) Reich et al (SGO 84 891 1947)

## LEISHMANIASIS

Among the protozoa, those which move by means of flagella comprise the class Mastigophora. *Leishmania* form a genus of Trypanosomidae the family which includes all flagellates living in the blood and tissues of human beings Leishmania have vertebrate and invertebrate hosts and, in their life cycle a leishmania and a leptomonas stage In the human host is found the typical leishmania, with ovoid body containing nucleus and kinetoplast the latter giving rise to a single flagellum in the invertebrate host. Reproduction occurs by binary fission The 3 species recognized as infecting man are morphologically identical despite the different clinical pictures produced by them.

Craig and Faust recommend their differentiation on the basis of serologic reactions. *L. donovani* causes visceral leishmaniasis or kala-azar. *L. tropica* causes cutaneous leishmaniasis or oriental sore. *L. braziliensis* causes American leishmaniasis.

**Oriental Sore** is a specific, ulcerative disorder which usually develops on the leg, face or other exposed part of the body. A small sore appears at the site of the bite of an infected sandfly, *Phlebotomus papatasii*, and the reddish papule increases gradually in size. After a number of months it becomes bluish in the center, softens, and ulcerates. The number of lesions ranges from 1 to 17, most often from 3 to 8; single sores are rare. The sore is not accompanied by adenopathy. After a duration of several months or even a year, an untreated ulcer undergoes cicatrization and leaves a characteristic stellate scar.



Fig. 433.



Fig. 434.



Fig. 435.

Fig. 433.—Oriental sore. (Dr. R. W. Mendelson. Thailand.)
Fig. 434.—Oriental sore. (Dr. C. L. Pickett. Philippine Islands.)
Fig. 435.—Oriental sore. (Dr. R. Simon. Java.)



Fig. 436.



Fig. 437.

Fig. 436.—*Leishmania donovani*, flagellated form seen in cultures. (Army Medical Museum. Mackie's *Practice of Medicine*. Mosby Co.)
Fig. 437.—*Leishmania tropica* in a smear from a tropical ulcer. (Army Medical Museum. Mackie's *Practice of Medicine*.)

Principal pathologic changes are in the dermis. The histologic picture is not distinctive, except that it is tuberculoid. The presence of Donovan bodies, representing apparently the specific parasite, readily demonstrable as a rule in Giemsa's stainings, is diagnostic.

The malady is self-limited, although its duration can be greatly shortened. Local treatment with wet applications and iodine help, and specific treatment with ½ gr. potassium antimony tartrate in 5 cc. water intravenously on one day, followed 3 days later with 1 gr. and continuing with 1.5 gr. a week, led to cures (Goodall: Ind. Med. Gaz. 72: 3, 1937). Snow et al. (AD&S 57: 90, 1945) spoke highly of Neostam in treatment, but Most and Lavietes (Med. 26: 221, 1947) preferred ethylstibamine (Neostibosan).



Fig. 438.



Fig. 439.

Fig. 438.—Tropical granuloma. (Dr F G Harris.)
Fig. 439.—Oriental sore (Dr E. L. McEwen.)









Figs. 440-442.—Leishmaniasis, Brazilian cases. (Dr O. G. Costa.)







Figs. 443-445.—Leishmaniasis, Brazilian cases. (Dr O. G. Costa.)

giving 0.3 Gm. intravenously daily for 17 days. Treatment failures may be retreated with *larger doses, or with Stilbamidine.*

**American Leishmaniasis** differs from oriental sore in its varied and longer course, its failure to produce immunity, the involvement of the nasopharynx in from 10 to 20 per cent of the cases, its greater resistance to treatment and the causation at times of cachexia and death. Oriental sore is a milder disease, confined to the skin, responding readily to treatment. See Fox (ADS 30: 241 1934; J 123 461 1943); Costa (ADS 49: 194 1944); Ball and Ryan (BullUSAMD Aug 1944)



Fig. 446

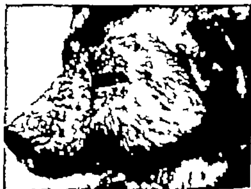


Fig. 447

Fig. 446.—Verrucose leishmaniasis, Brazilian case, rare type. (Dr O. G. Costa)
Fig. 447.—Leishmaniasis in a Peki mongrel. (Feng et l. ChinMJ 55 371, 1939)



Figs. 448-450.—Kala-azar nodules nd depigmented lesions in ll Indi ns. (Napier nd Dasgupta IndMGaz 69 121, 1934)

**Kala-Azar.**—This severe form of visceral leishmaniasis occurs in parts of India, China and the Sudan. It is a localized disease which may attack ll the persons in one dwelling o group of dwellings, and leave unaffected persons only a short distance away. All races and both sexes are infected. *Phlebotomus argentipes* is a vector, the bite or perhaps the crushed body serving to inoculate. After an incubation period of several weeks, kala za is manifested characteristically by an irregular fever lasting for months, uninfluenced by quinine with hypertrophy of the spleen and liver. In advanced

cases, numerous ulcers occur in various places along the digestive tube such as gangrene of the mouth, or ulcers of the nose or of the large intestine and on the skin. Wasting becomes advanced, contrasting with the protrusion of the belly which is likely to be distended with ascitic fluid. Cutaneous lesions, leishmanids, contain parasites. On the skin of the body limbs, or face appear depigmented zones, erythema, nodules, or more rarely verrucous, papillomatous lesions resembling those of xanthoma, with perhaps thickening of the lip eyelids, and also nasal. Evolution is insidious and may cover a period of 10 to 30 years. Cutaneous disorders are considered sequels of kala azar supervening in some instances in subjects who are ignorant of having had the malady. They may be mistaken for leprosy. Marked leucopenia, even to levels below 1,000 leucocytes per c.mm., is characteristic in the blood picture, the reduction of the polymorphonuclears being especially marked. The main visceral lesions involve the spleen, liver and large intestine. The tissue of the spleen is firm but friable and macrophages with parasites in them are found here diagnostic on splenic puncture. Sternal puncture is a safe way to obtain diagnostic material.

## TRYPANOSOMIASIS

**Trypanosomes** are flagellates which have a fusiform, fringed body containing two stainable masses of chromatin, one of which large and *generally centrally* located, is the nucleus and the other smaller and caudally located, is the blepharoplast. From it arises a whip or flagella, fastened along the body so as to produce an undulating membrane the anterior end being generally free. *T. gambiense* and *T. rhodesiense* cause African sleeping sickness. *T. cruzi* causes South American Chagas disease.

**Symptoms.**—African trypanosomes are inoculated by the bites of flies, most of which are members of the genus *Glossina*. The site *of inoculation, the bite is scarcely* distinctive, producing nothing more than a wheal which disappears rather promptly. The regional lymph nodes may exceptionally become enlarged promptly after the bite. Striking changes in the skin occur in European patients in the form of erythema multiforme like lesions of polycyclic and annular type. Among Negroes itching papules are more commonly seen. Areas of hypersensitiveness are found in a high proportion of the patients affecting both the skin and deeper parts the least blow or pinching *of deeper masses produces within a second or two such acute pain, peculiarly delayed,* as to make the subject actually cry out (Kerandel's sign). Generalized edema or true myxedema is a part of the symptom complex, and may be due particularly in the South American disease to actual damage of the thyroid gland. These cutaneous phenomena occur in the primary stage of the disease when hyperpyrexia and acute respiratory and circulatory symptoms are present. They may last for several months or years, with remissions.

## METAZOA

**Metazoa** of many kinds provoke eczematous dermatitis. Among the coelenterata, the Portuguese man-of-war provokes coryzal symptoms, pain, ulceration, and severe urticarial dermatitis by its sting, on contact with the skin, its venomous nematocysts (Thomas FlaMAJ 26 83, 1939). Jellyfish intoxication and dermatitis were discussed by Stuart and Slagle (USNMBull 41 497 1943) who noted similarity to black widow spider bite. They gave calcium gluconate 10 cc of 10 per cent, with prompt benefit. Zieman (J 99 1713 1932) advised drying immediately after contact and dry pressure dressings. See Evans (BMJ 166, 1943). Urticaria and contact dermatitis were reported from coral by Levin and Behrman (ADS 44 600, 1941) and from a hydroid by DeOreo (ADS 54 637 1946).

**Zoonanthoses** is a term proposed to cover those dermatoses caused by the introduction and retention of animal structures such as piercing mouth parts and bristles. Some are essentially foreign body irritants many of them are venomous rather than mechanical lesions. Immunity to metazoa may be manifested by encasement in fibrous tissue inflammatory expulsion from the gut antibody formation and cellular reaction; and more or less specific immunologic diagnostic tests have been devised (Taliaferro AmJTropM 20 169 1940, PhysRev 20 469 1940). See Culbertson (Immunity Against Animal Parasites, Columbia U Press 194_)

Urticaria and eosinophilia accompany many metazoan infections. Helminthiasis is capable of inducing malnutrition accompanied by xerosis and of vitaminosis A, pruritus and pellagra.

All metazoa parasitizing man are bilaterally symmetric. They fall into 4 phyla

| | | |
|---|---|---|
| Soft skinned | PLATYHELMINTHES (Flatworms) with body with or without segmentation celom obliterated. Digestive system if present usually lacks anus. | WORMS |
| | ANNELIDA (Roundworms) with body segmented celom present. | WORMS |
| Chitinous integument | NEMATHELMINTHES (Roundworms) with body nonsegmented no articulated limbs. | WORMS |
| | ARTHROPODA, segmented limbs jointed. | ARACHNIDS MYRIAPODS INSECTS |

## NEMATHELMINTHES

This phylum includes the true roundworms, or **Nematodes**. They possess an intestinal tract but no proboscis and the body cavity is not lined with epithelium. They are divided into Aphasmidia and Phasmidia depending on their lack or possession of phasmids which are caudal chemoreceptors. The Aphasmids include the Trichinelloidea, in which the anterior part of the body is filiform, esophagus degenerate, intestine cellular sexes hologonic, the female with single ovary polymyarian.

**Trichinosis.**—*Trichinella* contains the single species *T spiralis*, of which the adult worm inhabits the small intestine and the larvae emigrate into the muscles, here they become encysted. They infest the human being, cat, rat, dog, pig, and other animals. Cutaneous symptoms include in a small proportion of cases, a maculopapular exanthem resembling rose spots, scarlatiniform erythema, and erythema multiforme. Edema of the eyelids, photophobia, chemosis, subconjunctival petechiae, rose spots, and urticaria are common. Urticaria may be the first symptom. Splinter hemorrhages beneath the nails are petechiae due to larval migrations seen in some 60 per cent of active cases (McNaught AmJTropM 19 181 1939) Scarlatiniform eruptions were seen in 2 of 6 cases by Millett (BullUMdMSch 28 163 1944) The Bachman skin test using as antigen a dilution of saline extract of larvae is of interest. It does not become positive before the second week after onset of symptoms, and is an immediate wheal type of reaction when positive. Perhaps 10 per cent of reactions are false positives, and reactivity once established persists for years (Warren et al. AnIntM 13 2141 1940)

**Ascariasis.**—Phasmid nematodes of the superfamily Ascaroidea are fairly large, stout forms possessing a mouth with 3 conspicuous lips but without a buccal capsule.

*Ascaris lumbricoides* is a round, white, intestinal parasite ranging up to 10 inches long. Infestation is a cause of urticaria. Erythema nodosum has appeared in heavily infested children. Cutaneous allergy develops.

**Oxyuriasis.**—Phasmid nematodes of the superfamily Oxyuroidea are small forms, more or less pin shaped with buccal capsule and cuticular esophageal lining well developed.

*Enterobius (Oxyuris) vermicularis* adults are white worms 5 to 15 mm. in length called pinworms these inhabit the human intestine. The female with full uterus migrates toward the anus and thousands of eggs are laid in the dejecta and rectal mucus. Pruritus ani result from infestation. It is a symptom of remarkable periodicity appearing always in the evening at bed hour probably because of the warmth and quiet, which encourages great activity on the part of the worms near the anus. Erythema of the anal margin is seen, with many reddish points from the bites of the worms; there is considerable thick and sometimes blood tinged mucus, in which ova are to be found. Vulvar and vaginal involvement occurs. Diagnosis an anal swab is made of Scotch tape wrapped sticky side out about the closed end of a test tube. The sticky surface is rocked against the anus, the tape then pasted on a slide and examined for adhering ova (Jacobs JPed 1 497 1945)

Thymol is useful vermifuge. A dose of 4 grams may be given an adult, 1 or 2 to a child, dividing the dose into 0.5 gm. parts, giving one each hour. Follow the last dose with a saline purge. Hexylresorcinol crystoids, 1 gm. for adults and 0.6 to 0.8 gm. for children, are recommended. The dose is swallowed without chewing in the morning on an empty stomach. Gentian violet also is used internally (Wright and Brady: AmJMSc 198: 367 1939 J 114 861, 1940)

**Strongyloidiasis.**—Phasmid nematodes of the superfamily Rhabditoidea include the species *Strongyloides stercoralis.* The free-living generation lives in the soil, a roundworm roughly 1 mm. long and 60 microns in diameter. The fertilized female discharges embryonated eggs which hatch within a few hours, and rhabditoid larvae emerge, feed, moult and soon grow into free living adults. These may metamorphose in unfavorable conditions into filariform larvae resembling those of the hookworm and as such are infective for man, capable of remaining alive in the soil for many weeks. On contact with the skin or mucous membranes, they penetrate, producing a *petechia and intense pruritus at each site followed by edema and perhaps by secondary* infection. Some reach blood vessels, and are carried to the lungs, where they perforate the endothelium, enter the alveoli, induce a pneumonitis simulating bronchopneumonia, pass up the respiratory tree, and are swallowed. Reaching the intestine they lodge in the villi and crypts, mature, and deposit eggs. Diagnosis requires the identification of larvae in the feces. Gentian violet, enteric coated tablets of 1 grain taken three times a day for a fortnight, usually succeeds. See Simpson (J 113: 888, 1939) Craig and Faust (1945)









Fig. 431. Fig. 432 Fig. 433. Fig. 434.

Fig. 431.—Trichinosis, showing urticaria on chest and edema of face. (Dr J W Perkins.)

Fig. 432.—Splinter hemorrhages under fingernail in trichinosis. (Dr L. H. Briggs.)

Fig. 433.—*Living trichinella larvae* in sediment of digested human muscle (×13) (McNaught AmJTropM 19 181, 1939)

Fig. 434.—Encysted trichina in human muscle cells. (Dr J. B. McNaught.)

**Ancylostomiasis.**—Phasmid nematodes of the superfamily Strongyloidea include the Ancylostomatidae, the human hookworms, which are characterized by their possession of oral cutting organs, toothlike processes in the genus *Ancylostoma,* semilunar plates in *Necator.* Larvae of these worms may penetrate the skin, causing more or less severe irritation and dermatitis.

*Ancylostoma duodenale* common in Europe and the Mediterranean region, is a cylindric worm, 10 to 18 mm. long, which lives in the small intestine. The eggs, laid in the intestine of man, are passed with the feces and become larvae. After development, these larvae can penetrate the skin, circulate in the blood, and enter the lungs, whence, via trachea and esophagus, they reach the intestine to undergo evolution into adult form. *Necator americanus* is a similar parasite common in America. Penetration of the skin is not alone through hair follicles. The lesions in sections show dense eosinophilic infiltration. Itching, redness, and small pustules result from the percutaneous migration, which requires only a few minutes. Bacteria may be introduced into the tissues along with the larvae. Ground itch, miners itch, water itch, and



Fig. 485.—Creeping eruption due to *Ancylostoma braziliense*. (Dr O. G. Costa.)



Fig. 486.—Creeping ancylostomiasis in ol [illegible] boy' back. (D Grover Wende.)





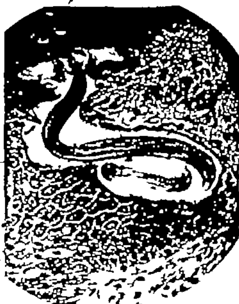


Fig. 48[illegible] —*Ancylostoma braziliense* ( [illegible] by histologic sections ) [illegible] epidermis. (Kirby Smith, Whit and Do[illegible] [illegible] 13 137 1926.)

mazamorro are lay names applied to the dermatosis. Cutaneous ancylostomiasis usually begins between the toes and extends over the foot. Itchy plaques and erythematous macules may be succeeded by vesicles, pustules, and ulceration.

Catarrhal bronchitis may symptomatically demarcate the passage of the larvae through the lungs. Eosinophilic pneumonopathy Loeffler's syndrome occurring in conjunction with cutaneous helminthiasis, represents an allergic phenomenon. Wright and Gold (J 128 1082 1945) observed in 9 of 15 cases of creeping ancylostomiasis transient migratory pulmonary infiltration with little or no sign or symptom of systemic disease except eosinophilia of the blood.

CREEPING ANCYLOSTOMIASIS.—*Ancylostoma braziliense* of which the dog is the natural host, causes, in its larval state a type of creeping eruption. The disease is common along the coast of the southern part of the United States. Infected cats or dogs inoculate the soil with their feces, and in moist, shady sand or earth mature filiform larvae invade the skin of human beings when opportunity offers. A reddish, itchy papule marks the site of entry, and within 2 or 3 days a sinuous tunnel in the epidermis has been produced. The lesion is first erythematous; it becomes elevated and vesicular. The larva moves several millimeters or even centimeters per day. The portion of the tunnel first made, and so first abandoned, tends to heal. Itching is severe. The number of lesions depends on the number of infesting larvae; tunnels may be solitary or numerous. Exposed portions of the body are the sites of predilection. A larva may persist with its wanderings for several weeks or even months (Dove AmJHyg 15 664 1932). The larva, located at the terminus of its tunnel, may be frozen in situ with the ethyl chlorid spray; this treatment is usually effectual. Cure may be obtained by intramuscular injections of Fuadin, 6.3 per cent solution 2 cc. daily for 5 doses, perhaps repeated after a week's rest according to Smith (J 123: 694 1943). Wilson (FlaMAJ 30 425, 1944) and Hitch (ADS 55: 664 1947) confirmed this, but Dolce and Franklin (ADS 52: 174 1945) reported disappointing results. A grated raw onion poultice applied thick, overnight for 3 to 7 nights, will do the job, wrote Hailey (SMJ 39 371 1946).

**Spiruroidea**, a superfamily of phasmid nematodes, contains several species of dermatologic interest. *Gongylonema pulchrum* has been reported in the Southeastern United States. Its eggs are ingested by beetles or cockroaches, within which they hatch and burrow and subsequently reach the mucosa of the human mouth, throat, or esophagus, where they tunnel and migrate. Mechanical removal of the threadworms can be accomplished. *Gnathostoma spinigerum* parasitizes the tiger and other hosts in the Far East. Eggs in feces hatch out motile larvae which enter a *Cyclops* and later a second intermediary host. In the human being, immature worms usually penetrate only superficially, producing stationary or migratory lesions which are abscesses or firm nodules with abscessed centers. *Thelazia callipaeda* is a parasite of the conjunctiva of dog, rabbit and man, occurring in China, Burma, and India. Other species exist which also evince predilection for the ocular region. Arthropodan intermediary host are involved and the adult worms, perhaps longer than 1 cm. and creamy white, coil in the conjunctival sac and migrate so as to produce severe pain, lacrimation, and irritation. They may be removed mechanically (Hosford et al AOphth 27 1165, 1942, *T californiensis*.)

# FILARIASIS

Phasmid nematodes of the superfamily Filarioidea are filiform worms with a simple mouth, almost circular, surrounded by papillae, lacking lips and with buccal cavity at most rudimentary. The adult lives in the tissues or body cavity of a vertebrate host. Eggs are partially embryonated before birth, and at about the time of oviposition the embryos uncoil as delicate snakelike microfilariae. These circulate in the blood or move in the cutaneous tissues and are ingested by blood-sucking arthropods. Migrating from the digestive tract of the arthropod vector they undergo metamorphoses, and mature larvae migrate into and down the hemocoelic cavity in the labium so as to reach the skin of the vertebrate host upon which the vector next feeds.

*Wuchereria bancrofti* (*Filaria sanguinis hominis*) is a creamy, slender, smooth skinned worm, the adult of which, several centimeters in length, live in the human lymphatic system. The microfilariae are 100 to 400 times as numerous in the blood at night as during the day although those of the South Pacific lack such periodicity. They measure 130 to 320 microns by about 10 microns in diameter. Their evolution continues in mosquitoes and they introduce themselves actively through the skin of the human being when the mosquito attacks. Several vectors in addition to the usual *Culex fatigans* have been determined.

Filariasis occurs in Hungary and Turkey the Far East, Burma, India, Indo China, and vicinity the Dutch East Indies, Philippines, northern Australia and Micronesia, North Africa, and northern South America. The hyperendemic areas of yaws and Bancroft's filariasis are notably coextensive (Craig and Faust) *W malayi* is a similar worm reported from the Dutch East Indies in association with elephantiasis usually of the *upper extremity*

**Symptoms.**—Early clinical manifestations of filariasis were clarified by Saphir (J 128 1142, 1945) providing a well-defined clinical picture. Saphir's patients were men exposed in a heavily infected area. Within 3 to 6 months insidiously progressive and intermittent complaints developed with feelings of numbness of an extremity particularly at night, followed by aching abetted by exertion and the discovery of axillary or inguinal lymphadenopathy Periodically recurring pains in axillary arm, groin, thigh, and scrotal regions ensued, and nocturnal orchiodynia was commonly experienced. By this time examination would reveal lymphatic and genital findings multiple slightly tender firm discrete, movable lymph nodes, axillary inguinal and femoral regularly and other sites occasionally and funiculitis, usually left-sided occasionally varicocele hydrocele and epididymitis. Funicular involvement was palpable as a peculiarly nodular tender thickening Microfilariae could not be demonstrated, and diagnostic skin tests were without value If the patient were removed from the endemic area, nothing further developed Anxiety especially concerned with potential harm to genital function was usual but such fear was groundless.

Progress of disease beyond the early stages is characterized by lymphangitis associated with a red streak and perhaps palpable enlargement of the vessel Dull red tense edematous, painful swellings occur in arms or legs. Urticaria and eosinophilia sometimes are met but not always. Swellings develop rapidly regress, and recur Fever and malaise may accompany these exacerbations. No case of elephantiasis developed in an American soldier and the hazard of the public occasioned by returning military personnel apparently is negligible See Thompson et al (J 129 1074 1945) Hodge et al (AmJMSc 201 207 1941) Coggeshall (J 131 8 1946)

Late stages are characterized by chronic hyperplastic changes in the skin and subcutaneous tissues, which are due to lymph obstruction and inflammation and which may result in enormous increase in size of the affected part known as elephantiasis.

Chylous effusions in the chest and abdomen are occasional late manifestations

**Sporadic Elephantiasis** may follow recurrent cellulitis due to ha temia or dermatophytid or it may be due to malformation or to other causes of lymphatic obstruction Luke (SGO 73 472, 1941) listed chronic enlargement of the leg under 6 headings congenital hypertrophy lymphatic stasis congenital or acquired, developmental venous retardation mixed venous and lymphatic partial obstruction arteriovenous fistulas, and miscellaneous. See Allen and Ghormley (AnnIntM 9 16 1935) Luke (SGO 73 472, 1941) on nonfilarial elephantiasis. See p 177

**Diagnosis** is justified in early stages in endemic areas on clinical *grounds alone. Exacerbations precipitated by* exercise are suggestive



Fig. [illegible].



Fig. [illegible].

Fig. [illegible].—Nonfilarial elephantiasis recurrent erysipelas. (Dr H. C. Baum.)

Fig. [illegible].—Elephantiasis, histologic structure showing edema and perivascular inflammation. (Dr Stuart Way.)



Fig. [illegible].—Wuchereria bancrofti microfilaria which has emerged from sheath. (Army Medical Museum, from Meakins' *Practice of Medicine* Mosby Co.)

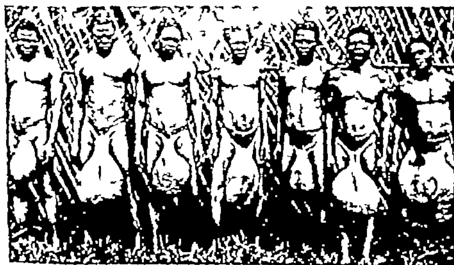


Fig. [illegible].—Filarial elephantiasis, 6 cases. Patient at left has hernia. (Dr L. F Jaggard.)

Proof of infection requires demonstration of microfilariae in the blood, lymph node, or hydrocele fluid or of a calcified worm by x ray. The skin test using *Dirofilaria immitis* antigen is of dubious value. Histologic changes are those of chronic inflammation nonspecific unless identifiable worm substance can be found (Michael USNMBull 45 225 1945).

**Treatment** during acute attacks should consist of rest and compresses and elevation if swelling and pain indicate their desirability. X ray therapy and surgery are not advisable then but elephantiasis may be attacked surgically. Neostibosan in increasing dosage reaching 300 mg on alternate days, may be given for a month or more; this by influencing adult worms diminishes the production of embryos (Culbertson et al. AmJTropM 130 534 1946). Anthiomaline may be useful (Brown J 125 952, 1944). Encouraging results with Hetrazan were reported by Stevenson et al. (J 135 708 1947) in doses by mouth of 0.5 to 2 mg./kg. t.i.d. for from 3 to 22 days. Avoidance of infected villages, mosquito control, protective clothing and bed nets and insecticidal efforts are indicated when one must stay where the disease occurs (WDTBM, no. 142, 1945).

## ONCHOCERCIASIS

Filarial worms of the genus *Onchocerca* inhabit connective tissues and blood vessels of mammals; in man they tend to accumulate beneath the epidermis. Black flies (*Simulium*) are the usual vectors.

*O volvulus* has a transparent, opaline body. The mouth is smooth. The male is 30 by 0.13 mm., with rolled up tail; the female reaches a size of 60 by 0.36 mm., and is viviparous. Both sexes are found in the subcutaneous tumors, which range from pea to pigeon's egg size and are located in scattered places, the popliteal, lumbar, intercostal, axillary, epitrochlear and nuchal regions. The tumors are sclerotic and contain adult and numerous embryo worms in canals in fibrotic tissue. They are generally readily enucleated, and they never occur in deep organs. The evolution is slow, the worm living many years. The tumors never ulcerate. Despite frequent exposure to infected bites, the natives in endemic zones may have only 1 or 2 verminous tumors; some sort of immunity may develop.

The embryos are some 300 by 6 to 7 microns in size; they have no sheath. They migrate in the connective tissue. They are much more numerous in the vicinity of the bite of a vector than elsewhere in the skin.

**Symptoms.**—In Mexico, especially Chiapas and Oaxaca, and Guatemala, infestation is common. Tumors containing *O volvulus* (*O caecutiens*) are almost always located on the head. Microfilariae in their migration are especially liable to enter the cornea, iris, and conjunctivae, so causing scarring and eventually blindness. Cutaneous lesions may resemble erysipelas in the acute phase. Chronic infection results in edema, eczema with hyperpigmentation and especially swelling of the ears.

Prevention consists in staying away from infested regions. If one lives there, one must destroy flies, avoid their bites, and excise verminous tumors as promptly as they appear. A strong solution of Apotheosine injected into the verminous tumor kills the parasites, renders excision unnecessary and relieves the symptoms of craw-craw (Strond, 1935). See Harris (TrRSocM&Hyg 34 233 1940), the disease in Kenya. Roberto (MMexic 24 263 1944) found wiggling microfilariae in split skin biopsy in saline. See also Goldman and Ortiz (ADS 33 79 1946).

**Filarial Itch** and other skin lesions are due to *O volvulus*. The former is one variety of craw-craw, a nonspecific native name. The dermatosis is not pathognomonic. It occurs in Central Africa, Ceylon, and China, and probably elsewhere. Papulopustules and plaques which may crust, ulcerate and leave scars are typical. The buttocks and flanks, the outer sides of the thighs, the elbows, forearms, and rarely the neck are involved; the face, genitals, and interdigital, palmar and mucosal surfaces are usually free. Repeated attacks occur and the eruption is therefore polymorphous. Urticaria may accompany the attacks. The dermatosis does not respond to antiscabietic treatment. It resembles dermatitis herpetiformis.

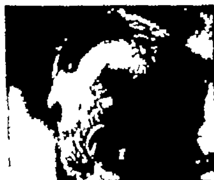


Fig. 442.



Fig. 443.

Fig. 442.—Onchocerciasis: verminous tumors of typical character and location in the Central American disease. (Strong et al.: Onchocerciasis, Harvard University Press.)

Fig. 443.—Onchocerciasis: the dermis in the pigmented plaques manifests cellular proliferation and infiltration and contains microfilariae. (Dr. R. P. Strong.)

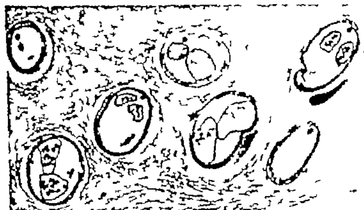


Fig. 444.—Verminous tumor of [illegible], showing O. volvulus adult worms. (Dr. [illegible])



Fig. 445.—Onchocercal dermatitis, erythematous, squamous and papular, showing microfilariae in the dermis. (Goldman: [illegible] 35: 355, 1948.)

## LOASIS (CALABAR SWELLINGS)

*Loa loa* has a transparent opaline body and a smooth, thick skin dotted with many small bosselations. The males are some 30 by 0.35 mm. (three times the size of *W. bancrofti*) and the ovoviviparous females are some 55 by 0.4 mm. They inhabit the subcutaneous tissue, and move about constantly so that little tissue reaction is present. Embryos are freed into the cellular tissues and enter the lymph and blood. They are some 250 to 300 by 6 to 8 microns in size. They are typically found in the blood in the morning, most numerous there shortly after noon, and they disappear in the evening. The mango fly is a vector.

**Symptoms.**—In equatorial Africa many natives harbor the parasite in the blood. The adult worm in its migrations produces egg size painless, warm swellings resembling angioneurotic edema. Where the skin is thin the outline of the worm itself may be visible. They have been known to traverse the conjunctiva. Itching, eosinophilia, and sometimes malaise and urticaria accompany the direct manifestations.

Antimony and Mapharsen are not effective but departure from endemic areas is followed by eventual relief (Guy et al.: ADS 47: 763, 1943).



Fig. 466.

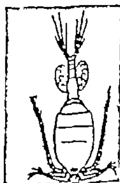


Fig. 467.

Fig. 466.—*Sparganum* larva of cestode, in eyelid of Annamite girl. (Dr. E. Brumpt.)

Fig. 467.—*Cyclops viridis* (×10) intermediate host of Dracunculus. (Drs. W. A. Riley and O. A. Johannsen.)

## DRACONTIASIS

*Dracunculus medinensis* the Guinea worm, produces a remarkable infestation observed about the west coast of Africa, upper Egypt, Asia, Persia, and India. The female is from 30 to 100 cm. in length and 1.0 to 1.7 mm. in diameter; the male, rarely discovered, is 2 to 4 cm. long. The worm lives in the subcutaneous tissues. The female develops, migrates, and appears in the skin several months after one ingests with the drinking water certain crustaceans, *Cyclops* infested with the larvae.

**Symptoms.**—Adult worms develop within the host, and the viviparous female makes her appearance after several months, laden with larvae, at the bottom of a pea-sized indurated, itchy lesion, the site of which is frequently the foot or leg, and through which larvae are extruded or she may form a soft, spongy cordlike mass under the epidermis. The parasites are usually solitary but may be multiple. The condition is relatively benign. Urticarial and asthmatic attacks and gastrointestinal upsets may complicate the infestation, often just preceding the development of the local skin lesion (Fairley and Liston: IndJMRes 11: 915; 12: 93, 347, 1924).

**Treatment.**—Emily injected 1:1,000 bichloride of mercury into the worm or the tumor it produced and after 24 hours the parasite could usually be extracted without trouble. The natives generally pull the worm out of its hole an inch or two and wrap it on a stick of wood. Each day some 3 or 4 centimeters of worm can be rolled up and with good luck a cure may be attained in a fortnight. Rupture of the worm during its extraction must carefully be avoided. Slaked lime 1:1,000 in the supply of drink

ing water repeated at intervals of 14 days or so, kills the cyclops. Boiling and filtering the water before drinking it are effective prophylactic measures. See Chitwood (J 100: 805, 1933)

## PLATYHELMINTHES

The phylum Platyhelminthes contains 4 classes, of which the Trematoda and Cestoidea include the human pathogens. Trematodes are exclusively parasitic organisms, the integument of the definitive stage nonciliated suckers usually present, circulatory system lacking, digestive canal present except in sporocyst generation of the subclass Digenea. This subclass contains the human representatives. Most of its species are endoparasitic, attaching by suckers, one of which is perioral, development is complicated, involving 3 or more generations and an alteration of hosts. The host harboring the intermediate stages is a mollusc. The order Prosostomata contains the flukes and schistosomes.

*Flukes.*—In *Fasciola hepatica* an illustrative trematod the egg becomes a miracidium, a free infusoria-like embryo. This, in the intermediary host, becomes a sporocyst which buds internally. These are freed and become encysted, and, in the liver of the definitive host give ris t the adult, which produces eggs. Cutaneous nodules, generally located on the trunk, occur rarely as rice-grain sized sacs conta ning 1 to 3 worms in a slimy jelly provocative of itching during the first few weeks of subcutaneous existence later becoming firm. Several species of worms cause similar tumors. Diagnosis can be made only after removal.

*Schistosomiasis.*—Schistosomatoidea is a superfamily of the order Prosostomata of the digenetic trematodes. The definitive stage is monoecious or dioecious, living in the portal blood streams of vertebrates. Cercariae enter the defin tive host through the skin. *S. haematobium* causes bilharziasis of the bladder; *S. japonicum* causes intestinal and splenomegalic involvement; *S. mansoni* causes intestinal and hepatic bilharziasis.

*S haematobium* cercariae penetrate within ten minutes when the kin is exposed to polluted water losing their bifid tails at the surface and entering the veins, where in about months they become adults, migrate to the bladder and produce disease there During the period of invasion, urticaria may occur along with the usual toxic fever, sweats, and malaise F brous nodules sometimes appear especially in the perineal and bathing trunk areas. Hard at first, they gradually enlarge soften, ultimately burst through the skin discharging thick, dirty caseous material. The sores generally persist as fistulas communicating with a deeper organ or mucous surface, simulating tuberculosi (Black BMJ 2 453, 1945) *S mansoni* cercariae penetrate the skin with the provocation of temporary sever pruritus and small papules, which appear within 6 to 8 hours afterward. Urticaria and purpura may occur (Hauser NOrlMSJ 93 663, 1939) Creeping eruption progressing 2 inches per hour along with crusts, urticaria, fever painful liver nd white cell count f 64,000 96 per cent eosinophiles, was reported by Wright and Roberts (EAf MJ 1 282, 1944) *S japonicum* infection resembles *S. mansoni*. Urticaria accompanied by fever may develop as early as the fifth day after exposure and about the end of the fourth week intense urticaria, subcutaneous edema, and large wheals affecting both skin and mucosae are usual, followed by toxic diarrhea. (Craig and Faust 1945; Faust et al AmJTropM 26 87 1946) The patient of F shbon (AmJTropM 26 319 1946) one week after exposure had angioneurotic edema of the face, chills, fever nd cough Pruritic papules appeared on the chest and became shotty grouped or coalescent Some developed postulation with ova in the pus. The lesions underwent fibrosis when Fuad n was given after ova ppeared in the stools

SWIMMERS ITCH —The cercariae f *Trichobilharzia ocellata* and other avian schistosomes cause a characteristic pruritic dermatitis of bathers in the Un ted States. Cort (J 90 1077 1928) recognized the nature of the condition when he experienced it himself as a result of immersing his forearms in water in which were recently collected snails. There occur (1) pricking sensation which may begin while still in the polluted water 2) rythema, papules, and sometimes pustules (3) intense rritation of the first few days, and (4) gradual disappearance f symptoms over a period of some 2 weeks. The orms a not parasites f man but rather f bird and mammals the eggs in the feces of these animal hat h m ater nt miracidia which develop into cercariae in snail See Brackett (J 112 11 1939)

*Cestoidea.* lass of Plat helm thes (cf T ematoda, above) are exclusi el parasitic organisms covered w th nonciliated integument adults hermaphroditic embryos hatched from eggs scolex provided with suckers and frequently with hooks fo attachment to host; no digest ve tract; body usually divided into separate, succes-

complete units called proglottids. The family Taeniidae of the order Cyclophyllidae of the subclass Cestoda contains *T solium* and *E granulosus*.

**Cysticercosis.**—*Cysticercus cellulosae* the larva of the cestode *Taenia solium*, causes in man small, rounded, firm, subcutaneous tumors, painful and larger while the parasite i alive and actively irritating but painless, smaller and sometimes calcified after its death. Rarely the lumps become abscesses. (Dixon and Hargreaves: QJM 13: 107 1944.)

**Echinococcosis.**—*Echinococcus granulosus* (Goeze 178_) lives in man only in the larval state. The adult worm is only 3 to 6 mm. long and inhabits the gut of dogs, particularly. The eggs reach the stomach of man by fecal contamination, and the embryos are freed. They generally infest the liver by way of the portal system, but may reach any part of the body. The cyst fluid is potently allergenic, and may be used for intracutaneous diagnosis (Culbertson: JClinInv 20 249 1941). The intracutaneous test sensitizes, and should be used but once. Some 8 per cent of cases of echinococcosi show subcutaneous lesions. Urticaria, fever, pruritus, erythema, and hyperhidrosis are among the cutaneous symptoms due to allergy. In subcutaneous tissues, the lesions are walnut to apple size semitranslucent cystic tumors. The treatment is excision exerting extreme care to avoid rupture of the parasitic cysts.

**Sparganosis.**—Pseudophyllodean cestodes of the family Diphyllobothriidae include spargana found in the subcutaneous tissues and muscles of various vertebrate hosts. Human infection may result from ingestion of larvae and their migration to subcutaneous tissues and further development there o from migration from infected flesh directly into human tissues. The worm are elongated ivory white ribbons, inducing in infected tissues edema, pain, and itching. The region of the eye is often involved i French Indo China.



Fig 468

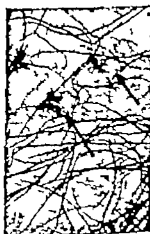


Fig 469.

Fig. 468.—Schistosome dermatitis. After exposure left foot was promptly wiped dry. (Brackett J 113 11 1939.)

Fig 469.—Penetration of follicle by cercaria causes and monetary papules. (Dr Laird Lyster Institut of Pathology McDonald College, Quebec.)

## ANNELIDA

Roundworms of this phylum include leeches, the bites of which are of dermatologic interest. The leech maintains the flow of the blood it sucks by introducing an anticoagulant albuminose hirudin into the skin (QMN J 132 184 1946).

## ARTHROPODA

The phyl m a th opoda con st f in rtebrat segmented, bilaterally s m metric animals. Their bodies are composed f more or less well differentiated part enclosed in a chitinous frame and the paired extremities are art culated. They possess

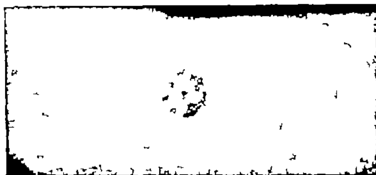


Fig. 470.—Insect bite on forearm. (Dr. Clyde Cummer.)

Fig. 471.—*A*, *Sarcoptes scabiei*, ventral aspect of female (×100). *B*, *Sarcoptes scabiei*, ventral surface of male (×100). *C*, *Pediculus humanus corporis* (×20). *D*, *Pediculus humanus capitis* (×20). *E*, *Phthirus pubis* (×16).

a complete digestive tract with mouth and anus, a blood system, a central nervous system with brain and with paired nerve trunks and ganglia for each segment, and separate sexes. The classes Arachnida and Insecta include all parasites of man. The class Diplopoda, millepedes, consists of fangless, nonvenomous animals with 2 pairs of legs for most segments. The class Chilopoda, centipedes, possess a single pair of legs per segment, the first pair modified to form poison claws. A Texas representative *Scolopendra morsitans*, can kill mice, and *S. cingulata* venom produces painful edema and papules in human beings. Urtication and purpura are approximately the worst they can do, and they are unable to bite through thick epidermis. Now and then one wanders into the nasal passages and sinuses. The class Crustacea contains a few copepods, such as *Cyclops*, which serve as intermediary hosts of worms of consequence to human beings.

Arachnida are terrestrial arthropods with tracheal or cutaneous respiration, the body being formed, in general, of 2 parts the anterior (cephalothorax) bears the mouth and 4 pairs of legs, and the posterior part (abdomen) includes the anus. Some members of the class bite or sting

Arachnida include the Arthrogastra, the orders of which have distinctly segmented abdomens (scorpions, pedipalpida, solpugida or pseudoscorpions, and harvest men) and the Sphaerogastra, spiders proper which lack distinct segmentation.

Scorpionida, true scorpions, are mainly tropical, they may reach a length of 8 inches and are pre-eminently predaceous creatures which lie hidden by day and hunt by night. Most true scorpions of the United States are of little significance, the sting of *Centruroides vittatus*, the common one for example being no more severe than that of a bee. *Centruroides suffusus* found in the southern part of the United States and throughout Mexico, is decidedly dangerous. Its toxalbumin, introduced perhaps into a bare foot, produces intense pain, numbness, sweating, salivation, rapid pulse shallow respiration, fever convulsions, and even respiratory paralysis and death, especially in children 1 to years old. Treatment of bites of venomous species is as for snake bites tourniquet and free excision. (Kent and Stahnke SMJ 23: 120, 1939.)

Pedipalpida, whip scorpions, are more feared than the facts justify Vesiculation has resulted from crushing a specimen upon the skin.

Solpugida are spiderlike forms lacking a true cephalothorax. The fangs can produce wounds, but venomousness is wanting

Araneida (spiders) and Acarina (mites and ticks) are orders of sphaerogastra arachnida.

## *ARANEIDISM*

All true spiders produce venom but few have fangs able to pierce the skin or venom potent enough to produce more than transitory irritation (Craig and Faust) The tarantulas, despite their dreadful appearance are essentially innocuous. The genus *Latrodectus* relatively small spiders of the family Theridiidae are the ones to be feared. Species occur in almost every country and *L mactans* the black widow is the member of consequence in the United States, southern Canada, Cuba Mexico, and elsewhere in the Western Hemisphere

*L mactans* is coal black with orange or scarlet markings. The male is about 6 mm long the female about 12 mm The abdomen is globose and has an hourglass-shaped reddish spot on its mid venter These spiders spin coarse tough webs about old lumber under outdoor privy seats, in garages and basements, and in trash piles, where they should be carefully avoided in order to prevent bites.

The bite is painful and the site becomes swollen and perhaps purpuric soon there occur general symptoms of intoxication including twitching and tremor numbness, vomiting sweating aching abdominal cramps that may falsely suggest the urgent need for surgery (Wilson Surg 13 974 1943) and even shock or delirium While the symptoms are sometimes exceedingly violent, actual fatalities have been few Atropine, intravenous magnesium sulfate morphine pituitary extract and epinephrine may be indicated Calcium gluconate may give immediate relief An antiserum

has been prepared and may be useful if given in time (Sharp and Dohme) See Kirby-Smith (SMJ 38 698 1945) Immediate incision and suction may be tried. One may flame the site of the bite at once with a burning match head and so prevent aftereffects (J 122 208 1943) Spraying the web with 10 per cent DDT in kerosene results in death of the spider (Van Riper Sc 104 111 1946) See Baerg (JParasit 6 161, 1923) Blair (AIntM 54 831 644 1934) Thorp and Woodson (Black Widow U N Carolina Press, 1945)

## ACARINE PARASITISM

Mites have globoid bodies formed by the fusion of the cephalothorax and abdomen. They have 4 pairs of extremities in the adult state the larvae are hexapod. The terminal segment of the legs possesses organs of fixation, hooks, claws, or pediculated suckers. Many are parasites Of the order Acarina, superfamilies containing members of dermatologic interest are Ixodoidea (ticks) Sarcoptoidea (itch mites) Demodicoidea (follicle mites) Parasitoidea (parasitoid mites) Tarsonemoidea (mites of grain itch) and Trombidoidea (chigger or red mites)



Fig 472



Fig 473

Fig 472 —*Demodex folliculorum* (Drs. Ayres Anderson and Foster)
Fig. 473 —Canine demodicidosis (sarcoptic mange) Inflammatory and foreign body reaction to mites in canine skin (Blaier JLCM 23 594, 1938)

**Demodicidosis.**—*Demodex folliculorum* var *hominis* is a minute parasite occurring in the hair follicles and sebaceous secretion in a considerable proportion of adults. The animal is cigar shaped measuring about 0.3 by 0.04 mm. Some believe it causative of some cases of rosacea, for in cases in which the organisms are numerous, clinical improvement along with their disappearance is obtained with sulfur ointment (Ayres ADS 1 19 1930) Others have incriminated it with the causation of tinea versicolor like discoloration of the skin and (rosacea like) impetiginoid, and rosacea like lesions (McAlynn ADS 43 43 1941 Nicholas Dh 47, 793, 1943)

**Sarcoptidosis.**—In scabies resulting from infestation with mites whose natural habitat is other than human the peculiar restriction and specificity of the relationship

of parasite with host is such that the acari do not thrive and multiply. Thus the burrowing by man of an animal mite may be unpleasant but it is not serious (Toomey UCutDis 25: 705; 26 473 1922)

*Tyroglyphus longior* the cheese mite has caused irritation of handlers of copra and cheeses. This resembles scabies or dermatitis venenata (Cleveland: ADS 41: 831 1940; Thomas: BJD 54: 313 194 ; Castellani: BJD 25 19, 1913 Saunders ADS 50: 45 1944) Tyroglyphid mites are world-wide in distribution and are sometimes present in flour sugar ham, meats, grain in mills, cereal foods hair upholstery mattresses, etc. (Anderson and Fishman ADS 5 : 227 1949) *Acarus farinae* (Linn) has caused severe itching in handlers of wheat; *Carpoglyphus passularum* (Hering) spoiled dates and prunes; *Glyciphagus domesticus* (deGeer) in grocers *Rhizoglyphus parasiticus* (Dalgetty) in Indian tea plantation workers.

## SCABIES

The itch, an infectious disease due to *Sarcoptes scabiei* var *hominis* is characterized objectively by intraepithelial burrows made by the female for depositing ova This results in intense itching and in multiform lesions due to scratching Secondary coccic infection is common.

*S. scabiei* var *hominis* (Linné, 1758) Female pearl gray or pinkish, about 350 microns long 300 microns across; oviparous. Male pinkish, about 225 microns by 175 microns. Venomous salivary glands open in the buccal cavity Ovum-bearing female inhabits the end of the burrow which she has made in the epidermal layer Male also may live in the burrow or more often outside the burrow under the epidermis. Eggs laid by the female measure 150 by 100 microns. Those farthest evolved are those farthest from the female located of course nearer the orifice of the burrow Development takes place in four stages (1) 7 days after being laid the ovum becomes a hexapod larva. It hatches in the burrow which it promptly leaves to live on the surface of the healthy skin. It enlarges and undergoes several moults. (2) By the sixteenth day the animal moults again and gives rise to an octopod nymph which lives in the crusts on the skin. (3) Another moult which occurs about the twenty-eighth day sets free pubescent male and female animals. (4) Following the final moult, which occurs about the sixth week, the pubescent and fecund female develops a new orifice which serves for the laying of eggs She then forces herself into the skin, producing a characteristic burrow in which she lays eggs. See Munro (JRoyAMC 33: 1, 1919) Warburton (Parasit 1 ?65 19?0) depicting varieties in ma ed animals, Buxton (Parasit 13: 146 1921 BMJ 397 1941) Friedman (Biology of Acarus scabiei, Froben, 194 ) Heilesen (ActaDV 26 1 Suppl. 14 1946, abs YBD 1948, p 400)

**Symptoms.**—Itching worse at night is the main complaint The areas of predilection are the dorsal aspects of the interdigital webs, flexures of the wrists, anterior axillary folds, lower abdomen, buttocks and genitals. In infants the palms and soles frequently are involved Other parts of the body also are occasionally attacked, but the face and scalp escape except in infants *The lesions, consisting mainly of small excoriated* papules and vesicles, are seen on close examination Tiny cuniculi or burrows can usually be found These appear as whitish tortuous or zig zag, superficial, threadlike channels. The closed end is marked by a tiny grayish speck the resting place of the female parasite The burrows are a few millimeters long and are most numerous on the interdigital webs, mammary region in women and shaft of the penis in men. *The disease is slowly but* steadily progressive as a rule and if neglected involvement soon becomes more or less general In cleanly individuals the eruption usually is scanty and impetiginous or urticarial manifestations may overshadow those of scabies. In neglected cases of long duration the number of acari may become enormous, with extensive crusting and the disease may involve not only the trunk, limbs, palms, and soles, but also the face and scalp (Norwegian scabies)

Figs 474 and 475.—Scabies

Fig 476.—Scabies typical excoriated papules.

**Diagnosis.**—The distribution of the lesions is suggestive. The hands may escape, but the anterior axillary folds in both sexes, the wrist, the nipple region in the female, and the shaft of the penis in the male should be scrutinized. *The interscapular region is free. In babies the soles, palms, scalp and flexures of the wrists usually are involved.*



Fig. 477 Fig. 478. Fig. 479.

Figs. 477 and 478.—Scabies in the infant. (Dr Robert N Andrade.)
Fig. 479.—Scabies, penile lesions. (Dr Sam Sweitzer.)



Fig. 480



Fig. 481.

Fig. 480.—Scabies interdigital lesions.
Fig. 481.—*Sarcoptes scabiei female* (×125) (Dr Fred Weidman.)

An infant lying in its crib rubbing its soles together probably has scabies (Dennie sign). Lesions may be limited to the penis (Gilman AD4 5 83, 1943). Exulcative erosion of the scrotum is usually scabietic. Scrapings examined in 10 per cent NaOH may enable one to identify parts of mites, eggs, moults, or scybala (Friedman PaMJ 47 39 1943). This technic is illustrated in the article of Hand (USNMBull 46 834 1946). With a dissecting microscope it is usually easy to obtain and demonstrate an acarus.

In pediculosis corporis, the parasite or its ova can be found in the seams of the underclothing, the hands and feet are unaffected, and the interscapular area is usually the site of numerous long excoriations. Nonscabietic dermatitis frequently involves the

palms and soles and the face. *There is no history of familial infestation, and acaricall are absent.* The distribution of the eruption seldom simulates that of scabies, and nocturnal aggravation of the itching is absent. Cutis anserina is almost constantly observed in the undressed scabietic patient. Errors in diagnosis arise from failure to suspect the infestation, or to recognize its complications, or to recognize it itself; interdigital and penile burrows, nocturnal itching, distribution of the eruption, and identification of the source are features one may depend on. Impetigo of the buttocks is practically pathognomonic of scabies (Stokes: J 106: 674 1936)

Epidemiology.—Close personal association and lack of cleansing facilities enhance the liability to infection. War conditions increase its incidence. School children pass the parasites to one another and bring them to their families. Mediate transmission probably does not occur and disinfection of clothing is unnecessary (Shand BMJ 1: 96, 1944) Clothing impregnated with DDT does not prevent one's acquiring *the infection (Hellier: BMJ 2: 253 1945) No significant difference was found in the* intelligence of scabietic and of other patients by Mellanby et al (Lancet 2: 596 1942)

Treatment.—The cure of a case of scabies depends on the external use of parasiticides. Impetigo due to scabies does not contraindicate such therapy Sulfur is a reliable agent and benzyl benzoate, betanaphthol, pyrethrum, derris derivatives, and other chemicals can be used successfully

The parasite is not hard to kill, success depending largely on the universality of application of parasiticide to the host, overlooking no solitary acarus. *S scabiei* is an obligate parasite on the human being It does not live longer than a *few hours on intermediary objects.* Overtreatment is to be avoided. A method we use may be outlined as follows

| | | |
|---|---|---|
| R | Phenol | 1.0 |
| | Salicylic acid | 6.0 |
| | Sulfur precipitated | 10.0 |
| | Petrolatum to | 100.0 |

Do not refill.

Fig Salicylic acid sulfur ointment for scabies.

1. Begin treatment with a hot bath, using nonmedicated soap generously *Dry* skin. Then rub in ointment gently from neck down covering the *whole* body palms and soles, fingers and toes.

2. Rub in ointment morning and night for 3 days [or 3] On the final morning take a soap bath, and change all clothing and sheets.

3. Use the same sheets and the same underwear until the third [fifth] sulfur application is finished and you have cleaned off the ointment. Launder everything, and start fresh. Ordinary laundering suffices. *Do not use more sulfur ointment unless so directed.*

Lesions may persist and itching continue despite successful attack on the mites themselves This persistence of irritability must not of itself be considered justification for a repeated course of the parasiticide for contact dermatitis would result It is to be allayed patiently with aluminum acetate baths, phenolated calamine lotion and barbiturates until 2 weeks have elapsed. Then if recognizable scabies still persist, the patient is retreated

Benzyl Benzoate (h. wever t eatment, Currey CanadPHJ 30 294 1939) (1) Use equal part of soft soap, isopropyl alcohol and benzyl benzoate. (2) Warm bath rub with soft soap, rinse (3) While wet, brush over whole body benzyl benzoate mixture for 3 minutes (4 Let it dry then paint t on again for 5 minutes. (5) Let this dry then put on some old clothes. (6) After 24 hours take cleansing bath and don fresh clothing Like ourselves Mellen (BMJ 452, 1942) prefers the aqueous emulsion. Graham (BMJ 1 413, 1943) obtained 89 per cent cures in 1,000 cases treated with a single application without disinfecting clothing. Geffen (BMJ 823, 1944 dispensed with both preliminary bath and scrubbing and attributed recurrences mainly to reinfection. *Aqua bentonite was the vehicle* and 2 per cent Duponol C the emulsifier for the 25 per cent benzyl benzoate preparation highly recommended

by Slepyan (J 124 11–7 1944) Dermatitis venenata may follow benzyl benzoate and is sometimes severe (Daughtry: J 1*7: 88 1945)

**Derris Treatment** (Saunders: BMJ 1: 624, 1941 1 1** 194 ): (1) Use 4 ounces of powdered derris root in 1 gallon of water (2) To a cupful of (1) add a dram of soap flakes apply over whole body 6 times in 2 days. One may dilute this to half strength to avoid irritation. Good when water is scarce nonodorous nongreasy no sterilization of clothing, no supervision needed, cheap, requires no skill to dispense. Epstein (ADS 45 950 194.) reported 15 per cent failures.

**Hexachlorocyclohexane**, the gamma isomer 1 per cent in cold cream, was successful in 93 per cent of the cases of Woolridge (JInvD 10 363 1948) The course of treatment consisted in a bath, inunction, 1 hour interval, inunction, L hour interval, final bath. This is available as Kwell (Commercial Solvents Corp.) Cannon and McRae (J 138 537 1948) cured 100 cases w thout irritation

**NBIN**—Carpente et al. (JInvD 7: 93, 1946): a spray of benzyl benzoate 10, DDT 1, benzocaine 2, Tween 80 (wetting agent) 2 water to 100 Topicide is Lilly's proprietary of approximately this excellent formula.

**Pyrethrum**.—Sweitzer and Tedder (MinnM 18: 793, 1935)

**Tetra Ethyl Thiuram Monosulfide (Tetmosol)** —Bradshaw (Lancet 271, 1944).

**Thiosulfate—Hydrochloric Acid** (Demyanovich's method: J 112: .378, 1939; 125 879 1944) (1) Shower bath with green soap and brush during which bathing is disinfected. ( ) Rub onto skin for 15 minutes a 40 per cent solution of the sulfate Dry with crystals of the salt Rub on 5 per cent solution of hydrochloric acid. (3) Repeat ( ) Cures 80 per cent in one treatment of less than hours.

**Complications** of scabies include secondary infection (impetigo ecthyma furunculosis, cellulitis, erysipelas, infectious eczematoid dermatitis) medicinal dermatitis venenata urticaria and dermographia insomnia, and psychosomatic reactions such as delusion of parasitism and neurodermatitis (Goldman WarM 5 294 1944) Secondary infection will not clear until the animal parasites have been eliminated after this has been done antibacterial medication is likely to prove unnecessary We have wasted some penicillin as well as antihistamine drugs on some cases of scabies, a disease not always textbook.

## CHIGGER MITES AND GRAIN ITCH

**Trombidoidea (Chigger Mites and Harvest Mites)** contain the famil Trombidiidae which are of medical interest These are scarl of silky hairiness, reddish in col r free and predatory as adults, a larvae parasitic on vertebrates and arthropods. The larvae known as *Leptus, or ha est mit s*, are fixed for v rious period of time on animals whose blood or lymph they suck. All larval trombid ts attacking man produce local phenomena and somet mes general intoxication, w th erythema of severity which varies with the species and number f parasites These ti y animals are common n the temperate zones and they att k usually are credited to the much rarer chigoe a flea Only the larvae are para t On cont ct ith the vegetation on which these are located, the skin is invaded. They ru t the rate f 10 cm. per minute and tend to attack themsel es on thin epiderm where they happen t meet an obstruct on such as a garter belt or brassiere They do not burrow Within a few hours they are engorged with blood and drop off (J 11 406, 1941)

*Trombicula irritans* (Riley 1873) is the chigger common n America. It is brick red in color and oval hape nd t measures from 0.3 t 0.5 mm by 0.25 t 0.3 mm. It lives n nature on woody decay ng substances and the fecal matter f arthropods, and occurs during J ly and August enormous under grass nd bushes, fields and moist swampy places.

*Trombicula* pecies tra smit J panese river fever and scrub typhus.

**Tarsonemoidea** cont in the mites predaceous on sects which ttack grain crops. *Pediculoid ventricosus* l es a parasit especiall on the larvae and nymphs f the corn moth. When t unable t attack these insect t passes ont th body f man and produces a polymorphous papular or papulovesicular erythema, accompanied t severe itchi g and sometimes by f er The parasites ttack people ork g with grain, particularly th e who unload t Rogers J 1*3 85 1943)

Harvest mites are abundant during the summer and autumn in some countries. The larvae attack the legs and accumulate in the regions of

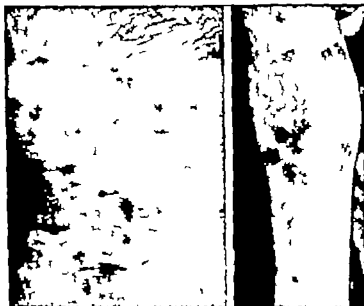


Fig. 482. Fig. 483.

Fig. 482.—Trombidiosis ("chiggers"): hemorrhagic, excoriated lesions on the thorax and abdomen. Vesiculation and fever may be present. (Dr. Howard J. Parkhurst.)

Fig. 483.—Trombidiosis: hemorrhagic lesions of leg, of six days' duration. (Dr. Parkhurst.)



Fig. 484.—Grain itch. (Dr. J. F. Schamberg.)

bands which bar their movement, such as belts and girdles. They force their rostrum into the skin, provoking severe itching and papules surrounded by a red or violaceous areola. These are soon excoriated. Even fever and insomnia may result. The acari live only a few days on man. The eruption produced by *P. ventricosus* is fairly well generalized and rapid in development. Schamberg (JCutDis 28 67 1910) described 3 clinical types: urticarial vesicular pustular the most common, varicelloid and erythema-multiforme-like. Itching has its onset after perhaps 24 hours. It is almost intolerable and is worse at night. Secondary infection is quite common as a result of abrasion. There may be malaise, some fever and moderate lymphadenitis. Urticaria is differentiated by the presence in grain itch of central vesicopustules. Varicella is less pruriginous, and the course of its eruption is more rapid. The lesions of scabies are different in character and distribution.

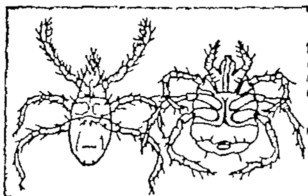


Fig. 4[illegible].—*Trombicula irritans* male and female larvae (×100). (Dr. C. V. Riley.)

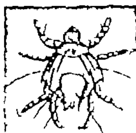


Fig. 436.



Fig. 437.

Fig. 436.—*Pediculoides ventricosus* male. (After Br[illegible].)
Fig. 437.—*Pediculoides ventricosus* gravid female. (After W[illegible]r.)

**Treatment.**—One should avoid exposure to the animals. Weak parasiticidal ointments, to which an antipruritic such as 0.5 to 1.0 per cent phenol has been added, prove comforting. Some harvest workers claim that they avoid infestation by taking sulfur by mouth. Immunity occurs in some persons, and mites are partial to others. Bathing with soap, applying to the skin a weak dilution of phenol in boric acid ointment and dust

ing the clothing with sulfur are procedures which yield some protection (Parkhurst ADS 35 1011 1937) Carbon tetrachloride, collodion or nail polish, applied to the bites, is comforting A repellent lotion containing 2 per cent rotenone is helpful (Williams et al. SM&SJ 103 199 1941) Various repellents successfully prevent infestation among the best of which are 6-12 and Kwell the active ingredient of which is hexachlorocyclohexane.

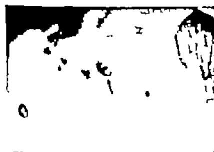
## RAT AND BIRD MITES

Parasitoidea is the superfamily containing *Liponyssus bacoti* the common rat mite and *Dermanyssus gallinae* a common parasite of fowls which may temporarily infest human beings. Rat mites transmit a rickettsial infection (q.v., p. 156) When efforts are made to exterminate rats, *L. bacoti* seek other blood, producing in human beings itchy wheals and papules with central puncta, especially on the extremities (Weber: J 114 1443, 1940 Riley: MinnM 23 423, 1940; Lowell: ADS 54 278, 1946) Insecticidal spray or fumigation with HCN will exterminate them. The rash may be mistaken for scabies. Fowl mite infestation results from the nocturnal activity of the animals, which migrate from abandoned nests of pigeon, starling, or sparrow as a rule. *D gallinae* is pear-shaped, about 1 0 mm. over all, grayish yellow and eyeless, able to run swiftly over the skin into which it does not burrow Infestation may be mistaken for delusion of parasitism.

## TICKS

Ixodoidea are large mites covered with a leathery integument and adapted exclusively to blood sucking from mammals, birds, and reptiles. The family Argasidae are soft bodied and the Ixodidae are hard bodied.

Ixodidae are vectors of great medical interest because in numerous localities they transmit to man various spirochetoses, rickettsiases, and tularemia; and they may cause tick paralysis, sometimes fatal, as well local inflammatory accidents.





FIGS. 488 and 489—Tick attached to skin, simulating seborrheic keratoma (Wiener J 113 1564, 1939)

Ixodidae are hematophagus in all stages of their evolution. They feed throughout the year or only at some seasons according to climatic conditions and their host's peculiarities. Each species seeks certain hosts by preference but, when these are not available, they content themselves with accidental hosts. The bite is always accompanied by some inflammation (Wiener and Strakosch JIn D 4 249 1941) *Dermacentor andersoni* is a vector of Rocky Mountain spotted fever and of tularemia, and is known to cause paralysis which is sometimes fatal (Abbott PSMMC 18:59 59 1943) *D variabilis* (dog tick) has been known to inoculate tularemia. *D occidentalis*, the Pacific coast tick, has transmitted tularemia

**Tick Bite Paralysis.**—Motor paralysis due to the bite of a tick and relieved by the removal of the tick has been observed in man and animals. The condition affects children as a rule There are observed weakness of sudden onset, ataxia, motor palsy clear conscious mental activity afebrile intoxication, and progressive paralysis

even to a fatal termination unless the tick is removed. Its removal is followed within 48 hours by recovery. *Dermacentor andersoni* is one agent, its venom rather than its function as a vector is apparently responsible. See Robinow and Carroll (J 111: 1093 1938); Abbott (PSMIIIC 18 39, 59 1943) Barnett (J 109: 846, 1937)

Argasidae.—Ticks of the genus *Ornithodoros*, some 30 species of which parasitize a variety of birds, mammals, and even reptiles infest nests and beds of their hosts, commonly dirt floored, thatched huts of man. They feed intermittently. Most of them bite painfully and provoke persistent, firm, itchy papules. *O moubata* inoculates African tick fever with its bite. *O hermsi* transmits relapsing fever in California. *O turicata* is the vector of sporadic recurrent fever in America.

**Treatment of Bites.**—One may touch the tick with tobacco juice kerosene, a hot nail, or one of the essential oils, thus inducing it to remove itself. The cutaneous lesions are urticarial and itchy but themselves inconsequential. Avoidance of tick infested regions is important in avoiding tick transmitted diseases (see p 155)

## HEXAPODA

In true insects, the adult possesses a single pair of antennae and 3 pairs of legs. The body is segmented and divided into head thorax and abdomen. Typically the thorax consists of 3 segments and supports 3 pairs of legs and pairs of wings, and the abdomen is composed of 10 segments the terminal one modified for sexual purposes. Some insects develop without metamorphosis, the adult developing from the nymph which hatches from the egg. Others undergo gradual, others partial, and still others complete metamorphosis in which the adult evolves from the pupa which has developed through several larval stages from the egg.

Insects perform their pathogenic services to mankind by mechanical and chemical external irritation by insertion of venom, by provocation of eczematous and systemic allergy by evolution and migration on, in, or under the skin, and by transmitting, inoculating and disseminating viruses, bacteria, fungi, protozoa, filariae and other animal parasites (Jarcho WarM 3 447 506, 1943)

Hexapodan Dermatoses include those due to the following orders:

| | |
|---|---|
| Orthoptera | grasshoppers, crickets, cockroaches |
| Ephemerida | may flies or shad flies, lake flies |
| Trichoptera | caddis flies |
| Mallophaga | biting lice of bird and mammals |
| Anoplura | sucking lice, pediculi |
| Heteroptera | bedbugs, assassin bugs, kissing bugs |
| Siphonaptera | fleas, parasites and mammals and birds |
| Coleoptera | beetles |
| Lepidoptera | moth and butterflies |
| Diptera | two winged flies, mosquitoes, botflies, houseflies |
| Hymenoptera | bees, hornets, wasps ants, ichneumon flies |

Orthoptera.—These are of little dermatologic significance. Grasshoppers can bite and fluid from some of them has been known to cause contact dermatitis.

Ephemerida.—May flies are included, and these may be heaped inches deep at times in the Great Lakes region. Asthma, urticaria, and eczematous dermatitis from crushing them on the skin have occurred (Figley J Allergy 11 376, 1940)

Trichoptera.—Caddis flies have caused asthma and urticaria.

Mallophaga.—These wingless, biting bird lice bite handlers of chickens, pigeons, and coops.

## PEDICULOSIS

Anoplura.—These wingless sucking lice parasitize warm blooded animals. Only the family Pediculidae re homin oxious. Pediculi of man, exclusively hematophagic insects, are specific parasites. Their voracity is considerable, and they eat or 3 times a day. They have little resistance to inanition and die in discarded clothing in a few days (Davidson MJ Austral 1 633, 1943) more quickly when humidity is low. The bite is disagreeable and itchy in persons who are not accustomed to it or who possess particular sensitivity. Lice are permanent parasites. Seasons have no influence on their generations, which succeed one another without interruption. The life span of

adults is perhaps 6 or 8 weeks. The resistance of the lice and their eggs to heat is relatively slight. In delousing the procedure must be conducted with care so that all parts of the clothing and coverings are exposed to adequate heat and drying.



Fig. 490.



Fig. 491.

Fig 490.—*Pediculus humanus corporis* (Dr Fred Weidman.)
Fig. 491.—*Phthirus pubis.* (Dr Weidman.)

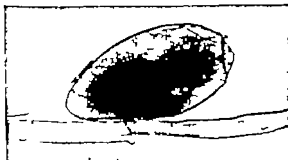


Fig. 492.—Nit of louse attached to hair



Fig 493.—Head louse and nit on hair (Dr O. G. Costa.)

*Pediculus humanus capitis* and *P. humanus corporis* interbreed without reduction of fertility; their biologic characters are intergradient (Nuttall: Parasit 11: 329 1919; Keilin and Nuttall Parasit 22 1 1930)

The head louse is grayish in color The male is some 1.8 mm. long and 0.7 mm. wide; the female is [illegible]7 mm. by 1 mm. It lives in the hair of the scalp, occasionally

in the beard. Rarely it is found in the pubic region. The female fixes her eggs or nits to the base of a hair. The young hatch on the sixth day and become adults on the eighteenth after having undergone 3 moults. Eggs may then be laid within a day or two.

The body louse is larger than the head louse and is dirty white in color. The male measures 3 mm. in length and 1 mm. in width; the female is 3.3 mm. by 1.15 mm. This louse is found on the skin only at the time of feeding. Ordinarily it hides in clothing or ornaments. It is cosmopolitan. It is a dangerous vector of typhus fever. While the exact method of transmission of this disease is not known, the excreta of the infected louse may be infectious. The spirochete, *Borrelia recurrentis*, of relapsing fever is transmitted from man to man by the body louse. See Buxton (The Louse, Wood, 1940).

*Phthirus inguinalis (Phthirus pubis)*. Forelegs delicate, with long, slender claws; other legs stout, with short, stout claws; thumblike process of tibia short and stout; abdomen short and broad. Nits are fixed at the base of hairs. Young hatch on seventh day and are able to reproduce 15 days after their appearance. The pubic louse is not known to transmit infection.

**Pediculosis Capitis.**—Children are more susceptible than adults. Itching is usually the predominant symptom. The presence of parasites and their ova is discoverable on close examination. Usually one finds exudative coccic dermatitis of variable severity, matting of the hair especially in the occiput, and lymphadenitis, especially of the posterior cervical nodes. Conjunctivitis was often present and corneal ulcer was not rare in the cases of Hirtenstein (BMJ 2: 75, 1943).

In treatment, clipping the hair is seldom necessary, although it facilitates the work. One application of Topicide (Lilly) will probably cure. A simple method of therapy uses the petroleum cap. The scalp is soaked with a mixture of equal parts of coal oil and olive oil (inflammable), then loosely bandaged. After 12 to 24 hours, the dressing is removed, and the head scrubbed with soap and water. Larkspur is satisfactorily employed in the same way. Way used 20 c.c. of xylol in 30 gm. of petrolatum. Tincture of cocculus indicus, 33 per cent in water, may be applied freely 2 or 3 times daily for several days, its use supplemented by frequent shampoos. Persistent nits may be loosened with weak washes of acetic acid (vinegar) or lemon juice and removed with a fine-toothed comb. DDT (dichloro-diphenyl trichloroethane) 2 per cent emulsion, one application without previous washing, is fairly reliable, but the animals die slowly. Worked into the scalp with a 2 inch paint brush, this is washed out the next day (Fraser, BMJ 2: 263, 1946). Davis (J 123: 8?, 1943) reported single application cures with phenyl or benzyl cellosolve 40 per cent, ethanol 30, methyl salicylate 5, and water to 100. NBIN, containing benzyl benzoate 68, Tween 80, 14 parts, ethyl aminobenzoate 12, and DDT 6, *to be diluted with water to one-sixth this strength*, is efficient for both lice and scabies (Eddy, JInvD 7: 85, 1946). Delousing of 1,500,000 persons in 45 days was achieved by dusting their underclothing with DDT 10 per cent in pyrophyllite with Flit guns (Ahnfeldt, JTennMA 37: 263, 1944). A second powdering a week after the first kills what hatches later. Kwell, containing hexachlorocyclohexane, may be recommended.

**Pediculosis Corporis.**—As a rule, the animal resides in and lays eggs near the seams of the clothing. It comes upon the body only to feed, commonly in the interscapular, shoulder and waist regions. Early lesions are minute, red, noninflammatory points, elevated but little. Usually the lesions quickly become papular and whealed. Excoriation leads to the appearance of bloody crusts. Itching is a prominent symptom. Secondary infectious manifestations frequently develop. In long-standing cases there

may be more or less brownish pigmentation Parallel linear excoriations in the interscapular region are almost pathognomonic. The bugs may withdraw sufficient blood to produce secondary anemia Among British troops in 1916 95 per cent of the men were infested, and they supported from 10 to 20 and even up to 1 000 cooties (Peacock BMJ 1 749 1916)

Experimentally lice caused at first only pi point, flat, red, noninflammatory lesions, but after a week and as a result of developing sensitivity reaction became papular with surrounding erythema and even vesicular reported Peck et al. (J 123 821 1943) Intradermal tests with louse antigen, that from feces being especially active, caused transient wheals in nonsensitive but tuberculoid reactions in sensitized individuals. The distress, widespread dermatitis, and psychic disturbance of the host were detailed by Ronchese (NEngJM 234: 665, 1946) Morris (NEngJM 233 160, 1945) attributed leg ulcers, in some instances to infestation. The rearing of a colony of lice was described by Culpepper (AmJTropM 24: 327 1944)



Fig 494 —Pediculosis corporis

The clothing must be sterilized. It may be autoclaved, ironed with a hot iron, dipped in naphtha or gasoline, or boiled. It may be fumigated with hydrocyanic acid, carbon tetrachloride or 10 per cent creolin solution. To discard and dry the clothing for several days suffices by starving the lice and desiccating the nits. Skin irritation and secondary infection may necessitate astringent baths, such as weak potassium permanganate In cases complicated with ecthyma and furunculosis, nits are usually present in the pubic axillary or perineal hair crop the hair change the kit, and remove nits with the application of paraffin and relief may be obtained.

**Phthiriasis.**—*Ordinarily the crab louse confines its activities to genital abdominal and anterior thoracic regions*, but it may involve the axillae eyebrows, lashes, and body hair of hirsute persons. Recognition depends

on discovery of the active, tiny reddish brown animals, or their ova attached to hairs, or the iron rust like spots of excrement. Cutaneous lesions and symptoms are like those occurring in pediculosis corporis. Infection can readily occur through contact with contaminated bedding and clothing as well as by intimate contact. The animal lives on the skin, not in the clothing.

Maculae caeruleae are rounded, slaty gray or bluish spots of pea to finger nail size, occasionally seen on the thighs, abdomen and thorax of heavily infested persons. They are due to introduction into the skin of salivary gland material of the lice and disappear after disinfection. *Fever and malaise, as well as this curious dyschromia* are *sometimes* observed (Safdi and Farrington AmJMSc 214 308 1947).

In treatment the parts should be clipped close but not shaved then washed with soap and water. Tincture of cocculus indicus, diluted with 3 parts of alcohol or water may be applied several times daily. Camphor 1 per cent in mineral oil is excellent. Mercury ointment is less satisfactory. DDT 0.5 per cent in cold cream, a single application to hairy parts below the neck, is simple and effective (Sutton, Jr BullUSAMD 4 45 1945). Kwell, containing hexachlorocyclohexane, may be recommended. When the eyelashes are involved, the patient is usually a child, and he requires a general anesthetic so that the necessary manual removal may be accomplished (Goldman ADS 57 274 1948).

## BEDBUG BITES

*Heteroptera is the order of true bugs. The families Cimicidae* (**Bedbugs**) and **Triatomidae** (**Assassin Bugs**) are of interest. Red wild bugs including the Triatomidae are blood suckers, capable of inflicting painful bites with local swelling or even generalized urticaria from the potent salivary toxin. The so called kissing bug accomplishes its bites without producing pain at the time (Arnold and Bell: HawaiiMJ 3 121, 1944). *Trypanosoma cruzi* infection is transmitted by bugs.

*Cimex lectularius* the bedbug is cosmopolitan. The adult is 4 to 5 mm. long by 3 mm. broad. The body is covered with short bristles and hairs. Its stink glands lie on the inner surface of the mesosternum. Its eggs are pearly white oval and about 1 mm. long and are laid intermittently over a long period in crevices of bed and furniture and under seams and loose wallpaper glued to the spot by a sort of mucilage. Adults have been kept in a closed vial for a year without food and have survived. They feed on other creatures if man is not available. Three or 4 generations a year in combination with their natural hardihood and inapparent bility to bird and other predatory creatures, make them a pest hard to conquer.

The bedbug makes cutaneous punctures in efforts to reach the capillaries, but it approaches the body only to feed, residing in crevices of *mattresses and elsewhere*. A *transitory wheal develops*, and this may be succeeded by a circumscribed purpuric lesion which persists for several days. Erythematous wheals of uniform size about that of the fingernail, three in a row with central red puncta are typical. The lesions are usually multiple and give rise to more or less itching and burning. The condition is to be differentiated from urticaria in which the eruption is generalized and more or less symmetric and the lesions do not present central puncta. Itching and burning can be relieved by carbolized calamine lotion. The history is strongly suggestive when the patient retires without lesions and awakes with new ones.

Bedbugs may be got rid of by (1) fumigation with HCN, burning sulfur, formol or other vapors, (2) raising the house temperature to some 130 F by shutting the windows and turning up the furnace, or (3)

hanging coal tar naphtha on cotton diffusion screens near the walls for 24 hours at 60 C. Mercuric chloride solution may be poured in cracks where the eggs are. (Cragg IndJMRes 11 449 1923.) Beds and springs may be torch flamed. Repapering, repairs of cracks, painting and DDT spraying are effective.

## FLEA BITES AND CHIGOE INFESTATION

Siphonaptera (Fleas) are insects which parasitize mammals and birds. They are wingless with highly chitinized and laterally compressed bodies. The legs are fitted for jumping. Mouth parts are formed for piercing and sucking. Their parasitism is not closely limited; a hungry flea is a desperate creature and its willingness to exchange hosts is the basis of its danger as a carrier. Their transmission of bubonic plague is notorious. *Xenopsylla cheopis* is the rat flea, especially important as the vector of plague and endemic typhus. Many other species bite man and may transmit disease. The flea exposed to strong light seeks to hide and if kept for several days in a narrow glass vial gives up his proclivity for jumping; these facts form the basis of his training for participation in a flea circus.

*Pulex irritans*, the common flea, is of practically universal distribution. Some individuals are apparently more susceptible than others to its attacks, and the severity of ensuing irritation is likewise variable, depending, apparently, on acquired hypersensitivity (Boycott Nature 118 591, 1926). Desensitization with flea antigen may be successfully accomplished (Hatoff J 130 850 1946). Injections of thiamin may prevent bites or diminish reaction to them (Eder APed 62 300 1945). Ordinarily the cutaneous lesion is a pale or erythematous, evanescent, itchy wheal, with a minute, reddish, hemorrhagic point at the site of puncture. Occasionally the manifestations may simulate purpura. To diagnose one may don white hose, sit in the dark, put on light suddenly and find the fleas on the socks. Camphor and essential oils generally exert a prophylactic effect in keeping the body free from the pests. Derris derivatives are valuable (One Spot Flea Powder). For the relief of the itching which in some instances is intense resort may be had to carbolized calamine lotion. Shaking out the bedding prevents the hatching of eggs. Where fleas are troublesome floors should be as bare as possible. Cedar oil and other oils used in floor cleaning will drive away fleas. DDT dusting and rodent extermination are control measures. Various repellents, such as Kwell, are effective.

*Tunga penetrans (Chigoe)* is the important species of burrowing fleas with short thorax. The abdomen of the gravid female bulges considerably. The fecund female fixes herself in the skin, forcing herself into it little by little. After sucking blood for several days, she reaches the size of the fruit of a mistletoe and her body encloses multitudes of eggs. The chigoe, almost completely parasitic, is indigenous to tropical America, and is occasionally encountered in the temperate zones. The primary cutaneous lesion is a shallow burrow, of which the opening is blocked by the last 2 segments of the body of the parasite which swells with blood. It usually attacks the feet, particularly the toes beneath the free margin of the nail. Secondary infection, extensive ulceration and even gangrene may supervene. The animal may be touched with turpentine or removed from the skin with the aid of a blunt needle. This should be done promptly before she burrows deeply and swells. Rupture of the creature while it is in the skin, or during the effort to remove it, is to be avoided with care. Wearing good shoes prevents infestation as a rule (Faust and Maxwell [illegible] 2[illegible] 94 1930).



Fig. 495.—*Cimex lectularius* (×20) (Gradwohl *Clinical Laboratory Methods and Diagnosis* Mosby Co.)



Fig. 496.—*Pulex irritans*. (Dr. R. B. H. Gradwohl.)



Fig. 497.—Chigoe infestation.

## BLISTER BEETLES

Coleoptera.—In this order no member is a true parasite. None inflicts a poisonous bite or sting, but several species have an epidermonecrotizing principle in their chemical composition, so that they provoke blistering.

Blister beetles are of the family Meloidae. The adults feed on flowers and foliage. Cantharidin is the volatile, crystalline substance to which the beetle owes its vesiculating property. It ranges from 0.4 to some 2.5 per cent of the dry weight of the beetle, and is soluble in ether, chloroform, benzene, and olive oil, but only slightly soluble in alcohol. *Cantharis vesicatoria* is the so-called Spanish fly, abundant in southern Europe and parts of Russia, where collectors, their faces and hands protected, shake them in the morning from the poplars, ashes, and lilacs where they feed in the early summer time, onto sheets, whence they are collected, killed, and dried. *Epicauta*, a potato beetle (not the Colorado potato beetle) is of this group. *Pomphopoea sayi*, sometimes a pest on peach trees in this country, may cause serious poisoning of man. Among the rove beetles members of the genus *Paederus* contain a blistering principle not cantharidin. The life cycle of the Meloidae is not completely known; the insects appear and disappear suddenly and are present in numbers with seasonal periodicity. *Seasonal bullous dermatitis* is a title under which this beetle disease has been described.

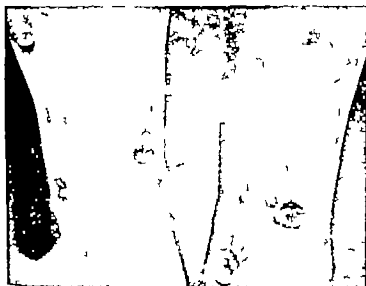


Fig. 118.—Blister beetle bullae. (Swartz and Wanamaker: J 131 594, 1946.)

The lesion which results from crushing an insect on the skin is a large, tense bleb, which itches and burns. While lesions occur on exposed skin, they also occur beneath the clothing where the insect may be blown by a gust of wind. Microscopically one finds in the lesion intracellular and intercellular edema of the epithelial cells, extreme in degree. Absorption through the skin may result in irritation of the kidneys. Benzene, followed by soap and water, will remove most of the vesicant, if used promptly. After the blister has developed it may be cut into from the side, and 1 per cent gentian violet in water may then be introduced into the cavity to prevent infection while the epidermis renews itself (Swartz and Wanamaker: J 131: 594, 1946; Huse: abs. ADS 42: 349, 1940).

## CATERPILLAR DERMATITIS

Lepidoptera is the order of moths and butterflies. Nettling hairs of the larvae of some lepidopterids provoke dermatitis perhaps as foreign bodies, probably as allergens, and certainly by virtue of poisons in them. No caterpillar bites or stings despite the wicked appearance of some of them, but some, innocent looking or even

attractive, have hairs which are highly irritating, while others have spines with spinules at their apices connected with underlying poison glands (Tyzzer: JMRes 11: 43, 1907) Hylesian moths irritated the patients of Hill et al. (J 128: 737 1949)

Caterpillar dermatitis occurring in Massachusetts and other parts of New England usually results from the nettling hairs of the caterpillar of the Brown tail moth many other species are also hominimoxious ( puss caterpillar, Lucas J 119 877 1942 brown tail moth, Steele and Sawyer MaineMAJ 35 157, 1944) The first manifestation is pruritus, which develops 20 to 30 minutes after contact. Erythematous macules soon appear usually followed by wheals. Cutaneous lesions are limited to the

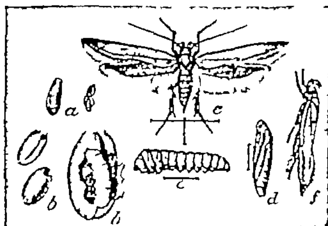
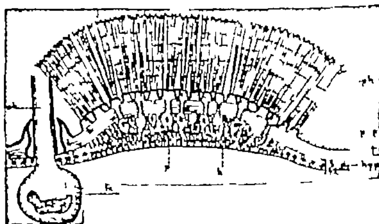


Fig. 499 —Brown-tail moth. (Webster.)


Fig. 500 —Brown-tail moth caterpillar section showing epithelium underlying nettling hairs. (Miss Kephart drawing, courtesy of Drs. Riley and Johannsen.)

area of inoculation The disorder usually develops during the months of May and June at a time when the caterpillars are maturing Numbness, nausea, and vomiting may accompany severe percutaneous intoxication. Conjunctivae may be affected as the skin is. Moths and butterflies are of the same immunologic group for skin testing purposes (Parlato JAllergy 3: 459 1932)

Contaminated clothing should be destroyed. The hairs are generally imbedded so deeply in the skin that considerable time must necessarily elapse before the irritant is disposed of. The application of 1:2,000 mercuric chloride lotion, followed by painting each spot with flexible collodion, is a useful measure.

## MYIASIS

Diptera (Flies) are insects with 1 pair of membranous wings attached to the second thoracic segment, the second pair of wings being replaced by minute, club shaped halteres; mouth parts adapted for sucking; metamorphosis typically complete. There are many kinds of flies, including *Musca domestica*, the common housefly. Some of them bite painfully; others transmit disease either as vectors or as mechanical conveyers, and the larvae of yet others can burrow in the skin. Taxonomy is complicated, and we merely list some families: Culicidae, mosquitoes; Psychodidae, sand flies, including the genus *Phlebotomus*, members of which transmit Pappataci fevers, Carrión's disease, and perhaps leishmaniasis; Chironomidae, biting midges, gnats, and punkies; Simuliidae, black flies; Tabanidae, horse flies and gad flies; Muscidae, including biting stable flies; Glossinidae, tsetse flies; Sarcophagidae, flesh flies; Oestridae, warble flies; and Oscinidae, eye gnats which mechanically convey infectious agents of lacrymal secretions, sweat and exudates.

**Creeping Eruptions.**—Three varieties of migratory animal infestation involve the skin: (1) those due to nematode parasitism (p. 351); (2) those due to acarine burrowers (p. 362); and (3) those due to larvae of flies, particularly of the Oestridae, *Hypoderma*, *Gastrophilus* and *Dermatobia*. Avoiding the ambiguity of "creeping eruption," we prefer the names "cutaneous helminthiasis" for the nematode diseases, and "cutaneous myiasis" for dipteran infestations.

**Cutaneous Myiasis** is the affection caused by development within the skin or subcutaneous connective tissues of dipterous larvae. The clinical aspects are varied.

*Dermatobia hominis*, the tropical warble fly, attaches its eggs to a mosquito from which larvae reach and penetrate the skin, where the larva feeds, grows, moults twice and within 2 or 3 months works its way out and falls to the ground to pupate in the soil. It causes furuncular myiasis.

*Gastrophilus species*, horse bots, produce creeping myiasis. *Hypoderma bovis* and *H. lineatum*, warble flies of cattle, produce furuncular and migratory lesions. *Oestrus ovis*, the sheep bot, deposits first stage larvae in the conjunctiva or naris, where they burrow and irritate. *Cordylobia anthropophaga* larvae invade the unbroken skin, where they remain for a week or so. *Chrysomyia bezziana* lays eggs on ulcers or accessible mucosa, the larvae being capable of eroding the bones of paranasal sinuses. *Cochliomyia americana*, the primary screwworm fly, lays eggs on injured or unbroken skin where hatching of larvae is prompt and invasion with the production of festering wounds soon follows. *Cochliomyia macellaria* sometimes infests exposed wounds. *Auchmeromyia luteola*, the Congo floor maggot, enters the skin of Africans sleeping on bare earth. *Wohlfahrtia vigil* deposits larvae on skin, mucous membranes or sores attracted by foul odors. *Sarcophaga* species infest ulcers. See Craig and Faust; Young (ADS 49: 309 1944); Smith and Rosenberger (AmJTropM 22: 450, 1942); Harrell and Moseley (BMJ 35: 720 1942 on *Dermatobia hominis*); Costa (ADS 50: 36 1944 on *Dermatobia cyaniventris*); Turner (BMJ 2: 11, 1945 on *H. bovis*); Cushing and Patton (AnnTropM 27: 539 1933 on *Cochliomyia americana*).

**Creeping Myiasis** begins with a painful subcutaneous nodule which moves in a continuous fashion, its course being marked by a red and ecchymotic line which disappears in a few days. The migration of the pain and of the red line are pathognomonic; the line is narrow, somewhat elevated, tortuous, whitish or pinkish, and threadlike and it marks the migrations of an immature larva within or just beneath the horny layer. Ordinarily the larva moves at a rate of from 1 to 10 cm. per day. When the larva is ready to depart, the tender spot remains stationary. A little tumor develops there. Its summit undergoes necrosis, and it discharges seropurulent liquid and the larva itself. *Hypoderma*, *Gastrophilus* and *Dermatobia* cause most of these cases. Injections of chloroform have been successfully employed in treatment.

**Subcutaneous Myiasis** is characterized by ambulatory tumors, the larvae eventually producing furuncular lesions from which they are discharged. Until that time they wander beneath the skin for several weeks or even months and give rise to fugacious reddish, sometimes edematous tumors.

**Furuncular Myiasis.**—The cutaneous tumor is the primary and only manifestation occasioned by the larval parasites. This is produced by larvae which have evolved at that location. When the larva becomes adult, it falls away spontaneously leaving a lesion which heals with a scar.

**Myiasis of Wounds and Ulcers.**—The eggs of *Lucilia* species deposited in a wound will hatch in a few hours, and the larvae will penetrate into the lesion and thrive there. This may occur naturally as well as experimentally. Purulent lesions, such a

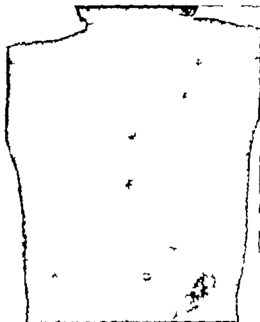


Fig. 501



Figs. 502–504

Fig. 501.—Furuncular myiasis due to *Dermatobia cyaniventris*. (Cort. AMA [illegible] 36, 1944.)

Figs. 502–504.—*Dermatobia hominis*: furuncular lesion, excretion of larva, and close up of the larva. (Harrell and Moseley, BMJ 35, 720, 19[illegible]2.)



Fig. 505.—*Chrysomyia macellaria* larva, pupal case and adult. (Dr. F. W. Shaw.)

syphilitic sores and other odorous ulcers, attract the flies. This form of myiasis is the most common. As a therapeutic measure, larvae of certain flies have been put into ulcers, for they eat decadent and purulent parts of the wounds without attacking healthy tissues. This method (Baer: JB&JSurg 13: 438, 1931; Maggot Therapy) has been used in America in many cases of osteomyelitis and other chronic affections.

**Treatment.**—In myiasis of wounds, one flushes away the maggots and picks them out with forceps as well as may be Chloroform, 15 per cent in vegetable oil, is efficient. A subcutaneous or intracutaneous larva may be killed in situ by injecting chloroform Hypersensitivity to deer fly bites was cured by desensitization with an antigen of macerated and Seitz filtered flies by Mease (J 122 227 1943)

## MOSQUITO BITES

Culicidae, the mosquitoes, are scale-covered dipterans which carry malaria, filariasis, yellow fever, and dengue. Species of *Psorophora* mechanically transmit eggs of the bot fly, *Dermatobia hominis* *Aedes aegypti* is suspected of mechanically transmitting the spirochete of yaws. Tularemia may be so conveyed Antennae of the males are plumed, and those of the females are almost smooth. The bite is painful and venomous. Species of mosquitoes too numerous to list inflict bites which become itchy wheals. Individuals differ in susceptibility and some apparently develop immunity Lesions resulting from bites may be classed as wheals which vanish quickly wheals followed by more persistent swelling, and bites which are followed a day later by red, itchy welts (Benson AIntM 64 1309 1939) Thiamin in adequate dose diminishes itching, papule formation, and susceptibility to bites, according to Shannon (MinnM 26 799 1943) Desensitization may be accomplished, the venom resembling that of bees (QMN J 120 726 1942) Repellents such as citronella are not very successful, but a DDT pyrethrin aerosol spray is. Meticulous control of breeding places, smudges, and protection with netting are necessary to control mosquito-borne diseases. Control likewise of infected persons must be considered in order to prevent the insects from becoming infected (Herms and Gray Mosquito Control Oxford U Press, 1940)

## INSECT BITES AND STINGS

Hymenoptera is the order which includes all the truly stinging insects, such as bees, hornets, wasps, and some of the ants. It is the abdomen of the female which is usually provided with a sting, or saw which is in fact a modified ovipositor and is connected with glands which secrete venom. Insect stings are inflicted only by the females.

Prolonged urticaria and even fatalities have been known to result from stings. Bees and wasps envenom as well as sensitize The swarming of bees upon the body and head may kill by suffocation. Violent motor response to stings, which are as startling as they are painful has led to cardiovascular death. That immunologic and allergic responses to insect proteins and venoms occur is indubitable. Passive transfer of sensitivity to bee venom may be accomplished but is imperfect for mosquitoes, and desensitization can be achieved with regard to the late papular reaction but not to the immediate wheal (Benson AIntM 64 1306, 1939) While the usual response to a sting is local swelling, redness and pain, systemic reactions may occur and generalized erythematous rashes have

been observed (Taylor BMJ 2 368 1939) At autopsy following bee stings, there have been found emphysema possibly with frothy exudation, overdistention of the right side of the heart and visceral passive congestion (Jex Blake EAfrMJ 19 74 1942)

One should lift out or scrape out the sting rather than pinch it by grasping it, a procedure which would force more poison into the wound. Local applications have little effect. Clad in black, one is more likely to be stung than if dressed in white Bumblebees do not lose their sting but can apply it repeatedly

Stinging ants are common in the tropics and those which lack stings have well-developed poison glands. Hornets and wasps are the more generally feared of the Hymenoptera some of the many species are of large size and are truly formidable

Cold moist compresses and antihistamine drugs by mouth may afford some symptomatic relief

## VERTEBRATE BITES

**Venomous Bites** are discussed in detail by Castellani and Chalmers (Tropical Medicine, Wood, 1929) Venomous fishes, including the scorpion fishes, rose fishes, and rock cod are discussed in BullUSAMD Jan. and May 1944. The lump fish, a spiny creature of the tropical Pacific, may even cause death. The sting ray stabs painfully with his barbed spine; see Evans (Sting Fish and Seafarer F ber and F ber 1943)

**Crocodiles** let go if the eyes are gouged (De Hartogh: JTropM 44: 11, 1941)

**Canine and Other Bites** liable to inoculate rabies should be irrigated at once and profusely with 20 per cent soft soap solution which is as effective as nitric acid according to Shaughnessy and Zichis (J 123 528 1943) Rat or cat bites may inoculate rat bite fever (q. v. p. 226) A *Pasteurella* infection with local and regional abscess formation and prolonged convalescence was described following cat bites by Allen (CanadMAJ 46 48, 194 ) See Hull (Diseases Transmitted From Animals to Man, Thomas 1941)

**Snakes** of various kinds are venomous, the hollow or grooved fangs providing the passageway from venom glands to victim. Kellaway (MJAustral 2: 585, 1938) described the various effects neurotoxic, with drunken incoordination, blunting of sensation, increasing drowsiness, dilation of pupils, slurring of speech, difficulty of swallowing, slowing of respiration, coma, and death preceded by convulsions; and hemolytic and cytolytic with edema, pain, purpura, salivation, oozing, blanching of skin, rapid shallow respiration and cardiovascular failure leading to death and coagulant such that in extreme poisoning the portal and mesenteric veins and vena cava may be clotted within a few minutes.

One cannot recognize the identity of the snake from the symptoms, which vary greatly depending on the dose of venom received Kellaway stated. One notes the distance between the punctures as indicative of the size of the snake One distinguishes the snap bite from the hold on type The thickness of clothing or absence thereof at the site is significant. A chance intravenous injection of venom rapidly fatal

Symptoms appear within a few seconds or minutes with nausea, vomiting, faintness, perhaps pain in the chest and abdomen. Albuminuria, hematuria, and hemorrhages from mouth, stomach, and bowel may be seen In the United States the pit vipers leave two small puncture wounds.

In treatment, Pender (PbMJ 15: 43, 1940) urged the application of a tourniquet an inch or two proximal to the wound prior to investigating the type of snake The tourniquet should obstruct venous but not arterial flow Cruciform incisions should be made through each fang mark, allowing free bleeding and suction should be applied to these for at least half an hour The tourniquet should be loosened for 1 minute of each 20 and may be moved proximally as the swelling increases. Antivenin is the best and surest measure when the specific type is promptly available according to Allen (BMJ 21 1 48 1938) who noted that time lost on it is practically useless, while excision as for carbuncle or even amputation may be requisite to save life. Local refrigeration offers only symptomatic palliation. Antivenin saves some

victims of the bite of the Indian krait, symptoms of which are colubrine, with saliva tion, coldness and prostration but without swelling or pain (D Abreu IndMGaz 74: 94, 1939)

The cottonmouth, copperhead, and rattlesnake are pit vipers; the brightly colored coral snake is the only other poisonous snake of the U.S.A. The pupils of the pit vipers are vertical slits. An adder is the only poisonous snake f England, but killed only 7 persons in the past 50 years wrote Walker (BMJ 2: 13 1945) Its bite causes massive edema, pain, and petechial hemorrhage, the victim being out of danger after 12 hours as a rule.

Cobra venom may be used therapeutically for the relief of pain in doses of 5 mouse units. Analgesia is slower but more lasting than that of morphine (Macht: MP&Circ 201: 254, 1939) It is of value in the palliation of advanced carcinoma (Maier: MWorld 57: 181 1939) Peck et al. (ADS 35 831 1937) discussed the use of moccasin venom in the treatment of purpura.

Human Bites assume medical importance because of infection which may occur in them from mouth organisms. Most cases result from fights or erotic agitation, but Butterworth (ADS 36 1162, 1937) called attention to those self infected by idiots, whose hands as a result show arciform hypertrophic and atrophic scars. In management, Maier (AnnSurg 106 423 1937) advised débridement, the operator alert to the possibility of injury to tendons. Liability to Vincent s infection requires early radical treatment, according to McMaster (AmJS 45: 60 1939) The wound is likely to be a small, jagged sore over the knuckle with swelling of the hand, cellulitis, and foul discharge when seen on the third or fourth day (Cohn Surg 7: 546, 1940) Virulent destruction, ankylosis, or amputation may succeed upon a seemingly trivial wound (Boland J 116 127 1941) Speirs (SGO 72 619 1941), discussing 114 cases, advised gentle but thorough cleansing with soap débridement only of damaged tissue, the avoidance of cauterization, excision, or the use of strong agents, and the applica tion of a dry sterile dressing. Probing and suturing are not advisable (Miller and Winfield SGO 74 153 1942) Penicillin should be given for a few days, and serologic tests should be done monthly for several months so that syphilis, if inoculated, will be recognized.

# DERMATOSES OF METABOLIC DISTURBANCES

## XANTHOMA

**Xanthoma** is a disturbance of lipid metabolism resulting in the deposition of oily substances in and between the cells of tissues including those of the skin. The deposits, discrete or diffuse, have a yellowish hue.

*Fatty Substances Occurring in the Human Body* (Aschoff: *Lectures on Pathology* Hoeber 1924) are:

1. Nitrogen free, phosphorus-free lipids, including
   a. neutral fats, which are glycerol esters with fatty acids;
   b. fatty acids and Na, K, Ca soaps formed from them (oleic palmitic stearic);
   c. cholesterin, a monatomic alcohol, $C_{27}H_{45}OH$ which may occur free or in esters
   d. cholesterin fats, combinations of cholesterin and fatty acids.
2. Phosphatides, which contain N and P and comprise esters of orthophosphoric acid, including lecithin and cephalin which are unsaturated, and sphingomyelin, which is saturated
   a. lecithin is the monoamino-monophosphatide stearyl oleyl-glycerophosphate of choline;
   b. cephalin is a monoamino-monophosphatide derivable from brain substance by *ether extraction, the base of which is not choline.*
   c. sphingomyelin, diaminomonophosphatide consisting of organic base, phosphoric acid and fatty acid, not extractable with ether
3. Cerebrosides containing N but lacking P which comprise glycol pins, including the galactosides cerasin and phrenosin.
4. Lipochromes and other fat-containing pigments, such as carotinoids and lipofuscin

**Types of Cutaneous Involvement.**—Two are recognized (1) **Xanthoma Tuberosum**, which is characterized by lesions predominantly on extensor surfaces, hyperlipemia, and frequent association with severe cardiovascular disease, especially angina pectoris and (2) **Xanthoma Disseminatum**, which is characterized by lesions predominantly on flexural surfaces and also mucous membranes, including those of the mouth, pharynx, and larynx, blood lipid levels within normal limits, and frequent association with diabetes insipidus.

Lipid Metabolism [illegible] related of course to ingestion for diets differ widely in chemical composition. It is related to thyroid function, for in hypothyroidism hyperlipemia exists, and in hyperthyroidism hypolipemia exists. It is related to pancreatic function, for many diabetics are hyperlipemic, and lipocaic (a pancreatic hormone, lacking which a depancreatized dog dies of fatty degeneration of the liver within 2 months despite insulin therapy) [illegible] concerned (Dragstedt et al.: AIntM 64: 1017 1939) And it is doubtless related t[illegible] ther hormones and functions which are not as yet understood Metabolic mechanisms are inherited to a greater or less extent. See Montgomery (JIn D [illegible] 325, 1938 AnnIntM 13 671 1939 MC[illegible] [illegible] 1940); Thannhauser (Lipidoses Oxford U Press 1940)

**Xanthoma Palpebrarum.**—The lesions consist of rounded, yellowish infiltrations in the skin of one or both lids of both eyes. Women are more often affected than men The lesions develop slowly and are at all times soft, noninflammatory and practically asymptomatic The disease is essentially one of middle or later life Palpebral involvement is frequently associated with the other forms of tuberous xanthomatosis, and moderate hyperlipemia occurs in about 7[illegible] per cent of the patients (Curtis [illegible]

55 557 1947) The lesions may be excised or neglected, or one can destroy them by means of the cautery or solid carbon dioxide. The scar of the burn does not contract but may be depigmented.

**Xanthoma Diabeticorum** is an eruptive, tuberous xanthoma which occurs in some cases of diabetes mellitus. The lesions exhibit a predilection for the buttocks, elbows, and knees. They are firm, solid, rounded, reddish yellow papules, from 0.5 to 1.0 cm. in diameter The lesions may be asymptomatic itchy or painful. They develop suddenly While generally discrete and few in number they may be numerous. After persisting for several months, or years, the papules may disappear spontaneously leaving no trace. Relapses are of fairly common occurrence. The patients are usually overweight and of middle age. The location of the lesions is influenced by trauma. They regress usually without a trace and fairly promptly on treatment directed against hyperlipemia (Garb: AmIntM 19 241, 1943) The serum is milky with neutral fat in these cases, but in xanthoma tuberosum the serum is usually not milky for neutral fat is only slightly increased, although cholesterol and its esters are elevated.

**Eruptive Xanthoma** is not limited in its occurrence to diabetics with hypercholesteremia (Combes and Behrman: ADS 48 927 1941) but is seen in xanthomatous biliary cirrhosis, xanthoma tuberosum and tendon sheath xanthoma if excessive hyperlipemia is present. Lesions may occasionally be papulopustular They contain neutral fat, fatty acids, cholesterol and other lipids. Hyperlipemia and the diabetic sugar tolerance curve may be detected by studies of the chemistry of the blood. Recovery is the rule and can be hastened by control of the diabetes, if it is present, which should be accomplished with the generous use of insulin and a diet not too rich in fats. Low fat diet and thyroid are likely to be helpful.

**Xanthoma Tuberosum.**—The lesions are widely disseminated, and the eruption which is more or less generalized in character may consist of papules, tubercles, nodules, and even tumors, often intermixed with plaques and striae The sites of predilection are the elbows, hips, and knees, although no region is exempt On the palms and soles the lesions, because of their peculiar saffron color stand out in bold relief. Rarely the nodules coalesce, forming tumors several centimeters in diameter Their consistency ranges considerably but as a rule they are soft. They develop slowly and seldom involute although spontaneous regression has been noted. Mucous membranes may be attacked Familial prevalence occurs.

Tuberous xanthomas are occasionally solitary Their firm, rounded, orange colored noninflammatory nodular character distinguish them from other tumors (Charache AmJCa 31: 604, 1937) They are not limited to cutaneous distribution, but occur within joints as pedunculated tumors attached to the synovial membrane, usually of the knee (DeSanto and Wilson JBJSurg 21 531, 1939) causing pain, stiffness and non malignant tumor Tendon sheath and synovial membrane cases were collated by Galloway et al. (ASurg 40 485, 1940) Such lesions were of low growth, firm, not tender and occur in feet, ankles and hands at about age 40 the location sometimes being determined by trauma. About 1... per cent recurred after excision Dupuytren's contracture affecting the medial palmar fascia and causing scarlike flexion of the fifth finger is possibly of xanthomatous nature (Meyerding et al. SGO 72 582, 1941) This condition may respond to vitamin E, Anderson (1947) told us

**Nevoxanthoendothelioma.**—Tuberous xanthoma in 5 infants was reported by McDonagh (BJD 4 85, 191..) in the patient of Lamb and Lain (SMJ 30 685 1937) the lesions involuted as the years passed and on the scalp produced permanent, striking alopecia. Such cases are notable for the remarkable clinical appearance of the coppery or lemon-colored papules, nodules and tumors, which are usually more pronounced on the upper half of the body The patient's health is little affected, although

the blood cholesterol and total lipid are much increased (Zeisler: ADS 40 626, 1939). Solitary lesions are seen occasionally (Fishman: AmJSurg 49: 456 1940)

**Extracellular Cholesterosis.**—The first patient (Urbach: DMtschr 66: 371, 1933 *YBD 1934*, p. 241) was an old woman who had progressively enlarging reddish blue nodules on the dorsum of the hands, soon also on the arms, later on the knee, thigh, ears and on the tongue, finally scattered over the chest, arms, and buttocks in violet patches and xanthic papules. There were also hypertension and cardiac decompensation, and the spleen and liver were enlarged and firm. The case reported by Layman (ADS 35: 269 1937) was a girl of 16, whose eruption had begun at the age of 5 years with vesicles which became papules. Some small lesions seemed to coalesce, especially on the



Fig. 506.



Fig. 507

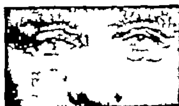


Fig. 508

Fig. 506.—Tuberose xanthoma. (Dr F R Burns.)
Fig. 507.—Xanthoma nodules in skin of thumb.
Fig. 508.—Tuberose xanthoma of elbow (Dr F G Harri )



Fig. 509.—Eruptive xanthoma, typical lesions of knees. (Dr T C Gilchrist.)





Figs. 510 and 511.—Xanthoma palpebrarum (xanthelasma)

backs of the hands, the knees, and about the ankles. Brownish violet mottled pigmentation, atrophy and scarring developed, scattered over the buttocks, thighs, and legs. The histologic and chemical findings were those of extracellular cholesterosis, foam cells and giant cells being absent.

**Resorption Xanthomas** comprise processes described as degenerative or inflammatory cholesterosis, where the xanthoma formation is local, and the lipoids, free locally are stored there by lymphocytes or connective tissue cells. This has been observed in the scars of syphilitic gummas, of laparotomy wounds, and of herpes zoster (Weidman



Fig. 512 —Eruptive xanthoma in a diabetic. (Dr Philip F Shaffner)



Fig 513 —Extracellular (nodular) xanthoma (Laymon ADS 35 368, 1937)

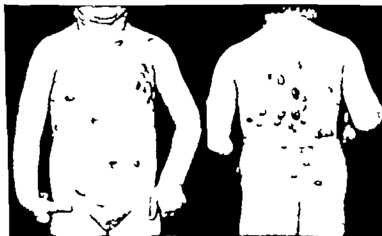


Fig 514 —Juvenile tuberose xanthoma (Lamb and Lain SMJ 30: 883, 1937)

and Boston: AIntM 56: 793 1937; Netherton: ADS 51: 100 1945) A case manifesting curious, chronic, fat-containing nodules on the extremities was described by Urbach and Hill (ADS 41: 150 1940) as lipid imbibition of degenerated collagenous tissue.

**Gaucher's Disease** (Large-Celled Splenomegaly Cerebroside Histiocytosis) is characterized by occurrence in children, familial tendency and insidious onset with anemia and xanthomatous (kerasin) splenomegaly and hepatomegaly. Hemorrhages sometimes occur. The skin gradually develops brownish pigmentation but xanthomas do not develop in it. Pingueculae are usual accompaniments. Lipoid deposits in the bones may be found on x-ray examination. A chronic course leading to death is to be expected.

**Niemann-Pick Disease** (Phosphatide Histiocytosis) is a disease of infancy occurring generally in Jewish individuals. It is characterized by brownish pigmentation of the skin, malnutrition, retarded development, hepatosplenomegaly of pronounced degree, decreased fragility of the red blood cells, leucocytosis of 10,000 to 40,000, and lecithin deposition in the parenchymatous organs and lymphoid system. The course is acute and fatal (Pick: AmJMSc 183 601, 1933).

**Skin and Mucous Membrane Lipoidosis With Hepatosplenomegaly** was described on the basis of the 1 case, a boy of 11 who had small firm yellow nodules on the face and extremities present since birth. Histochemical changes differ from those found in lipoid proteinosis, which this condition closely resembles. Differences from the Niemann-Pick disease are not great. There is tremendous hyperlipemia, with or without jaundice, along with lesions present on the mucous membranes which must be distinguished from those of xanthoma disseminatum. There is frequently marked increase in free cholesterol and also in lecithin, in both the blood and tissue lipoids (Urbach: KlinWchr 13: 577 1934).

**Hand-Schüller-Christian Syndrome.**—The first recorded patient with the combination of defects of the membranous bones, exophthalmos, and diabetes insipidus was that of Hand (APed 10 673, 1893). Some 30 per cent of the cases prove fatal. Arrest of development leading to dwarfism is a feature additional to bone defects, exophthalmos and diabetes insipidus, Atkinson (BJChildDis 34: 28 1937) judged from his survey of 103 cases. All the features of the disease need not, and generally are not, present in a particular case, and symptoms and signs vary according to the situation of the lesions. Defects of the cranial bones are an almost constant finding, while exophthalmos and diabetes insipidus are less constant. Diagnosis is made, he stated, by clinical picture, histologic examination, and roentgenograms, which alone may be distinctive; but changed blood lipoid levels are not diagnostically requisite. Yellow infiltrations of skin, mucous, serous, tendon sheaths and fascia along with infiltrations and nodules in liver, spleen, lungs, heart, lymph nodes, marrow and glands of internal secretion were observed by Lane and Smith (ADS 40: 617 1939) who listed cutaneous manifestations as including bronze pigmentation, maculopustular and hemorrhagic eruptions, and seborrhea-like involvement of the lids. The primary pathologic lesion is composed of reticulo-endothelial cells, singly or multiply nucleated, filled with lipoid, along with foreign body giant cells, eosinophiles, round cells, and young fibrous connective tissue cells. Old lesions are composed mainly of foreign body giant cells, fibrous tissue, necrotic tissue and cholesterol crystals. While in Gaucher's disease the lipoid improperly metabolized is a kerasin and in Niemann-Pick's disease a lecithin, in this condition, it is a cholesterin compound (Wahl: J 107 422, 1936). Some benefit has been obtained with dietary treatment, pituitary extract, and x-ray treatment (Kennedy: PSMMC 13: 776 1938).

**Letterer-Siwe Disease.**—Interpreted as a lipid reticuloendotheliosis related to the Schüller-Christian syndrome, this disorder is characterized by granulomatoid proliferation of the reticuloendothelial cells, which become filled with cholesterol. Infants are affected, and the disease may run a rapidly fatal course with hemorrhages and progressive enlargement of the lymph nodes, liver, and bone marrow. In older persons the course is slower and the granulomas which develop tend to involve the skull, orbital bones, spleen and liver (Abt and Denenholz: AmJDisChild 51: 499, 1936; Wallgren: ib. 60 471 1940). The case described by Cole (ADS 56 1—, 1947) was a male born with petechiae, whose skin developed crusted and bullous lesions. The spleen and liver were hard and enlarged, the abdomen tender and distended and the clotting time prolonged. The eruption was mainly on the trunk, comprising telangiectases, scattered papulosquamous lesions, small vesicles, crusted areas and scars.

**Dermatofibrosis Lenticularis Disseminata and Osteopoikilosis** appears to be related to xanthomatous, although it has long been confused with scleroderma, and may



Fig. 515



Fig. 516

Fig. 515.—Hand-Schüller-Christian syndrome. (Horsfall and Smith QJM 4 37 [illegible].)

Fig. 516.—Histologic lesion of Hand-Schüller-Christian case shown in Fig. 515. The granuloma is composed of large pale-staining cells with foamy lipoid-filled cytoplasm and vesicular nuclei; many multinucleated giant cells contain lipoid also.

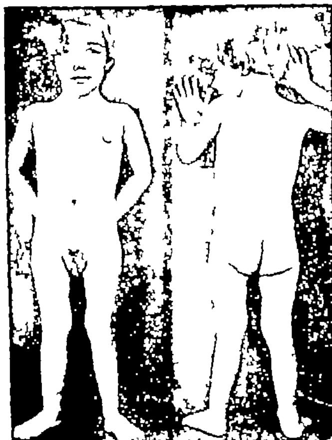


Fig. 517.—Osteitis fibrosa disseminata. (Albright et al. N Eng J M 216 727 1937.)

be a form of neurofibromatosis (Curth: ADS 30: 55-, 1934). The papular fibrotic lesions of her patient were uniformly pea-sized, firm, slightly raised and of normal color and they underwent no evolution. The eruption is usually papular sometimes purpuric. The eruption in conjunction with osteopoikilosis, the other element of the syndrome is diagnostic.

**Polyostotic Fibrous Dysplasia (Albright's Syndrome. Osteodystrophia Fibrosa)** is a rare condition in which patchy pigmentation is associated with asymmetric cystic bone disease. The patient of McCune and Bruch (AmJDisChild 54: 806, 1937) had symptoms at the age of 2 years, and began to menstruate at that time. Pathologic fractures are common. Albright et al. (NEngJM 216: 1937) described 5 cases characterized by multiple systematized bone cysts, apparently related areas of pigmentation, precocious puberty and occurrence in females only. Hyperparathyroidism was not present.

While the disease is of unknown nature there are similarities to xanthoma and to von Recklinghausen's disease. It occurs in both sexes, it is now known, but gonadal dysfunction is seen only in females (Dockerty et al.: AIntM 75: 33, 1943). Blood calcium is normal, and only scattered bones are affected, a distinction from hyperparathyroidism (Gorham: NYSJM 43: 415, 1943). Albright (JClEndocr 7: 307, 1947) thought his disease not xanthomatous because blood cholesterol is not abnormal, and the bone lesions progress only slightly, clear spontaneously and are not radiosensitive. The segmental distribution of bone and skin lesions, which do not coincide in location, is against a metabolic etiologic agency. The serum phosphatase level is high when the disease is widespread. He thought it not of the nature of neurofibromatosis because the latter does not induce increased as well as decreased bone formation in the same person or effect sexual precocity, while the former does not run in families. See Lichtenstein (ASurg 36: 874, 1938) and Edit. (J 135: 923, 1947).

**Necrobiosis Lipoidica** occurring not exclusively in patients with diabetes mellitus, is characterized by asymptomatic plaques usually located on the lower extremities. Well developed lesions are generally oval plaques, with well-defined borders and a smooth waxy surface. The central portions of the lesions may appear somewhat sunken and atrophic, or they may be xanthic and telangiectatic, becoming coppery and of cartilaginous texture. The outer zone is frequently violet. The surrounding skin is normal. The common location is on the lower extremities especially in the region of the ankle. The onset is insidious and the chronic course is asymptomatic throughout unless ulceration occurs.

The condition appears histologically to be the analogue of mild, abortive, superficial diabetic gangrene (Michelson and Laymon: ADS 35: 1130, 1937). Changes occur primarily in the dermis, where diffuse but patchy infiltration is seen with fibrotic and lymphocytic elements. Elongate and horizontally disposed necrobiotic masses of collagen appear pale and homogenized, and Sudan staining reveals diffuse fat in these and droplets about them. Elastic fibers are absent within the areas and are sparse, clumped, and fragmented in the vicinity. Vessel walls are thickened and there is proliferation of the intima with occasional thrombosis. While similarity to granuloma annulare exists, the two diseases can be distinguished histologically (Ellis and Kirby-Smith: ADS 45: 40, 1942. Laymon: Trans. ADA 1947). Blood lipids are elevated (Rattner: IllMJ 3: 339, 1939). A patient with hepatic and vascular disease but without diabetes was reported by Belote and Welton (ADS 40: 857, 1939). Of 78 Mayo Clinic cases reviewed by Hildebrand et al. (AIntM 66: 851, 1940) 8 were non-diabetic and 80 per cent were females.

No satisfactory therapy had been determined prior to the report of Burgess and Pritchard (ADS 3: 603, 1949) that vitamin E, 250 mg per day appeared curative. Diabetes if present should of course be well controlled.

**Lipoid Degeneration of the Elastin (Cutis Rhomboidalis Nuchae).**—In persons whose occupation has long exposed them to the atmosphere and actinic influences, the exposed skin may become furrowed and divided into rhomboidal and triangular fields. The texture becomes thickened and the color pale yellow or brownish. This change, characteristically involving the sides and back of the neck, may extend over the backs of the hands, the face and perhaps somewhat over the chest. The disease seems to be a primary degeneration of the elastic tissue. Colloid degeneration of the conjunctiva is frequently present (Kogoj: abs ADS 53: 59, 1946). The skin is vulnerable and purpura may follow mild trauma, even that of sunshine. Injury of the nail readily provokes, in the presence of this degeneration, purpuric streaks (Berlin: BJD 58: 274, 1946). The disease is essentially asymptomatic and little can be done about it (Urbach: YBD 1944, p. 314).

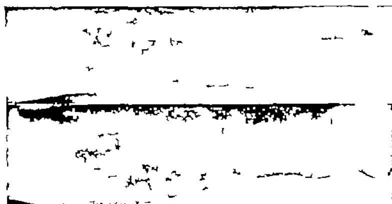


Fig. 518.—Necrobiosis lipoidica (Eckler and Caro ADS 30 794, 1934.)



Fig. 519.—Necrobiosis lipoidica in a diabetic.

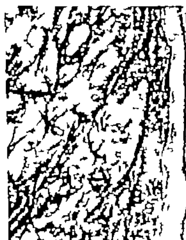


Fig. 520



Fig. 521.

Fig. 520.—Tuberous xanthoma showing foam cells.
Fig. 521.—Necrobiosis lipoidica, histology



Fig. 522



Fig. 523



Fig. 524

Fig. 522.—Diffuse xanthoma lipoidosis cutis et mucosae. (Wise and Rein AD&S 37 201 1938)

Fig. 523.—Diffuse xanthoma, sudan III stain of frozen section. N te lipoidal mantling of vessels and absence of giant cells. (Montgomery and Havens.)

Fig. 524.—Diffuse xanthoma, H. and E. stain of paraffin section. Note homogenization of collagen and perivascular clear spaces whence lipoid has dissolved. (Montgomery and Havens AOtol 29 650, 1939.)



Fig. 525.—Xanthoma tuberosum foam cells are the large clear ones. (Dr Fred Weidman.)

**Lipoid Proteinosis (Lipoidosis Cutis et Mucosae).**—Urbach applied these titles to a rare familial and congenital disease clinically manifested by infiltrations into the skin and mucous membranes consisting mainly of lipoid deposits. Hoarseness results from the pharyngeal and laryngeal involvement, and is usually observed in early infancy. According to Montgomery and Havens (AOtol 29: 650, 1939) cutaneous lesions may not appear until much later. There is usually a pocklike eruption on the face appearing in infancy and leaving soft, depressed scars. Extensor aspects of elbows, knees, and fingers are frequently involved and the scalp may show only a sparse growth of hair. The mucocutaneous junctions are affected, as are the labial, lingual, buccal, pharyngeal and laryngeal mucosae. There may develop the necessity for laryngotomy to prevent asphyxia. Some patients show indications of diabetes, and, while roentgen therapy is of no use, diet and insulin have seemed to help a few cases.

Microscopic examination reveals lipoid sheaths about the blood vessels of the skin and mucosae, and massive lipoid deposits in the cutis in the nodular type, or keratotic formations in the hyperkeratotic type. *There are no foam cells. The lipoids* are acetone-soluble phosphatides. A protein-lipoid combination is found in the deposits. *See Urbach and Wiethe* (*AfpathAnat* 273, 285 1929); Wise and Rein (ADS 37: 201, 1938); Wile and Snow (ADS 43: 134, 1941) liver damage and amyloid also present; Sulzberger (Laryng 52: 286 1942) 29th case; Ramos e Silva (ADS 47: 301, 1943), bullous and pustular lesions, histochemical studies showing protein-phospholipid hyaline in superficial dermis; Price et al. (ADS 55: 42 1947)

**Xanthoma and Visceral Disease.**—Throughout the preceding descriptions, note has been taken of the systemic aspects and influences of lipid disease. *Cutaneous xanthomas are occasionally associated with hepatic disease*, especially with obstructive jaundice due to stricture of the common duct, whether inflammatory or neoplastic. Cutaneous xanthomas are usually secondary to the hepatic disease. The xanthomatous lesions appear light yellow in contrast with jaundiced skin. Despite marked hepatic damage, as evidenced by clinical observations and liver function tests, the normal ratio between cholesterol and cholesterol esters frequently remains undisturbed. *There may be neither relative nor absolute increase in free cholesterol* but relative or absolute increase in phosphatides (lecithin) is likely to occur and there is hyperlipemia. *Palmar lesions* are present in practically all cases of hepatic disease associated with cutaneous xanthoma. Disturbances in melanin pigmentation of the skin may also be encountered. We have seen this respond promptly to thyroid extract. Hyperlipemia carotinemia xanthosis, or xanthochromia, and increase in the concentration of bilirubin in the serum do not *necessarily* parallel one another or correspond. Cutaneous xanthomas associated with hepatic disease may undergo involution *as the condition of the liver* apparently improves. Eruptions of red, circumscribed nodules which crusted centrally in 48 hours and healed with scarring and pigmented areolas were reported in a case of cirrhosis by Truffi (abs BJD 52 373 1940)

Occlusive arterial disease of the legs may be associated with tuberous xanthoma (Barker AnnIntM 12 1691, 1939)

Xanthoma is recognized as a cause of sudden death because of its relation to coronary disease. Müller (abs J 113 662, 1939) reported families in which angina pectoris was associated with xanthoma. He thought that xanthomatosis causes a special kind of arteriosclerosis distinguishable from the usual form. Hypercholesteremia is present but hypertension is infrequent. A family of 9 brothers and sisters, of whom 5 were xanthomatous and 4 died suddenly between the ages of 6 and 23 years, was recorded by Bloom et al. (ADS 45 1 1942). *Young men with coronary disease*, xanthoma, and hypercholesteremia were studied by Engelberg and *Newman* (*J* 122: 1167 1943)

**Etiology Pathology and Treatment.**—The causes of lipid disturbances are incompletely known. Xanthoma tuberosum represents irritative connective tissue hyperplasia due to extravasated lipid. The presence of lipids in the cells does not appear to affect their vitality but makes them foamy in appearance. Probably any cell capable of phagocytism is capable of becoming a xanthoma cell, which is a histiocyte modified by the storage of cholesterol esters. Giant cells are common. During regression such cells may come to resemble those of spindle-cell sarcoma. Lesions have been produced in the skins of rabbits by feeding the animals cholesterol (Rusch et al APath 28 163 1939). Instructive articles are those of Montgomery and Osterberg (ADS 37 373 1938) and Wilder (AIntM 61 297 1938). Hypercholesteremia is heritable with or without xanthoma, stated Fliegelman et al in a genetic study of a large family (TransAMA, June 1948).

While diet helps in hyperlipemic xanthomatosis, the production of xanthoma in normal persons does not result from limiting them to a ketogenic diet (carbohydrate 25 gm fat 200 gm., protein 60 gm.). It seems that the reticular cells may either make or store cholesterol, and in xanthoma they are unable to get rid of it. To encourage elimination restriction of animal fat in the diet medication with thyroxin, iodides, and garlic and, in nonlipemic deposits, x radiation may be useful therapeutic measures. When xanthomatous tissue forms despite the existence of a practically normal level of lipemia as it does in the disseminated forms in contrast with the eruptive forms, little may be expected. Cardiac damage eruptive xanthoma and low BMR were the features of a patient much benefited by Delp (JKansMS 41 95 1940) by low fat diet and thyroxin. Vitamin A 200 000 units, and 0 5 gm dehydrocholic acid daily yielded an excellent result for Montgomery (ADS 51 214, 1945) in 1 patient.

## CAROTINEMIA

**Carotinoid Pigmentation** is the dermatologic manifestation of this metabolic error. The region of the nasolabial folds and the palms and soles are the sites of predilection affected in mild cases when severe pigmentation is generalized excepting the sclerae (Heymann AmJDisChild 51 273 1936). Carotinoid pigments color the blood serum account for 30 to 60 per cent of the color of plasma and fix themselves in the fat of the dermis and subcutaneous tissue and in the keratin of the epidermis and sebaceous gland (Jeghers NEngJM 228 678 1943). Cutaneous changes generally result from overingestion of lipochromes, which are richly present in orange carrot egg yolk, and other brightly colored foods (Rattner and Olnsberg ADS 40 831 1939 Rosen ib. 44 730 1941). Carotinoid pigmentation is seen also in diabetes, xanthoma, and myxedema (Boeck and Yater JLCM 14: 1129 1929; Almond and Logan BMJ 239 191 Escamilla JClEndocr 23, 194). In distinguishing carotinoid pigmentation from jaundice Cameron (NCarolMJ 5 432, 1944) noted that in carotinemia pruritus does not occur the sclerae are clear the urine is less dark and does not contain bile the blood bilirubin is not increased and the stools are normal. A test devised by Greene and Blackford (MCNAm 10 733 1926) consists in overlaying the serum protein in a test tube with alcohol which dissolves the bilirubin and then with petroleum ether which takes up the lipochromes. In treatment the diet should be altered to exclude yellow substances and thyroid given if indicated.

## PSEUDOXANTHOMA ELASTICUM

This rare affection is characterized by aggregations of flat yellowish, intracutaneous abnormality in an ate circumscribed, and diffuse plaques forming patches symmetrically located in the flexural fold axillae, sides of the neck, upper and inner aspects of the thighs and over the abdomen in extensive cases. The lesions are

asymptomatic but persistent. Angioid streaks of the retina occur in about ..3 per cent of the cases the association of skin and retinal changes being known as the Grönblad Strandberg syndrome (Urbach and Nekam: KlinWchr 13 857 1936). Angioid streaks were ascribed to degenerative rupture of the elastic membrane of Bruch by Urbach and Wolfram (AfDuS 176 167 1937) in whose patient similar damage of the aortic elastica was also found at autopsy. Benedict and Wagener (AmJMSc 203: 801, 1943), Hagedoorn (AOphth 21: 774, 935, 1939) and others have confirmed such an explanation, but Ebert (ADS 45: 75, 1943) denied that satisfactory elucidation of the nature of the streaks had been achieved. Histologic study of the skin shows that the plaques consist of alteration in the middle and lower dermis only where circumscribed regions contain clumps of swollen and degenerated elastic fibers and basophilic degeneration of the collagen. Giant cells and xanthoma cells are absent. The epidermis may be slightly atrophic. The cause and cure of pseudoxanthoma elasticum are unknown.

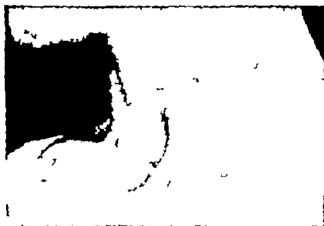


Fig. 326.—Pseudoxanthoma elasticum (Dr D. E. H. Cleveland)



Fig. 327.—Pseudoxanthoma elasticum taken f how degenerated elastic tissue Weigert hematoxylin ... tissue stai (Throne nd Goodman ADS 4 419, 1921.)

Famil al incidence sometimes occurs, as the sister reported by Shepard (ADS 4.. 898 1940). Usually harmless, the disease has nevertheless been found causative of ... retinal hemorrhages, and even blindness (Hubler ADS 50 51 1944). Revell and Carey (SouthMJ 41 ... 1 48 t essed the ... aspect f the dystrophy of elastic tissue the ... f which are named pseudoxanthoma elasticum. Hypert nsion, ... f pulse calcification of peripheral

vessels, and abnormal bleeding into the gut, uterus, bladder and brain have occurred, and the incidence of thyrotoxicosis and diabetes mellitus seems abnormally high in these patients.

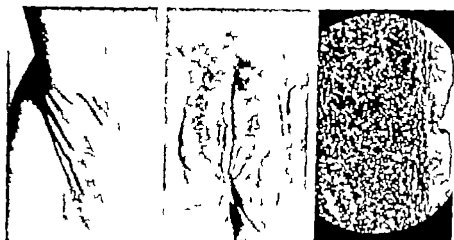


Fig. 528 Fig. 529

Fig 528.—Pseudoxanthoma elasticum of axilla and vulva. (Dr O G Costa)
Fig 529—Pseudoxanthoma elasticum, histopathology (Dr Stuart Way)



Fig. 530—Angioid streaks of retina. (Dr Cecil O'Brien.)

## URTICARIA PIGMENTOSA

Urticaria pigmentosa (xanthelasmoidea) is characterized by the occurrence of yellowish or brownish pigmented lesions which manifest urticarial irritability when mechanically stimulated. The disorder is comparatively rare. Since the review by Graham Little (1906) Finnerud (ADS 8: 344, 1923) was able to find 15 additional

cases. The disease generally begins in early infancy with the appearance of wheals, papules and nodules which may not at first be differentiated from those occurring in urticaria of the ordinary type. Cases fall clinically into the 3 varieties: macular nodular, and mixed. The nodular type is suggestively similar to xanthoma. Scarring on involution is rare but is associated especially with the nodular lesions. Lesions may be present at birth (Boardman ADS 43: 670 1941) resembling nevoxanthoendothelioma (q. v.) Bulla formation sometimes occurs (Tave: ADS 55: 558, 1947)

Cases in adults characteristically present mild urticarial symptoms, the lesions being small, macular or almost macular and often telangiectatic (Barber and Weber: InternatClin 4: 71 1937)

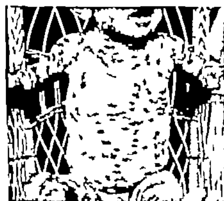


Fig. 431.



Fig. 432.

Fig. 431.—Urticaria pigmentosa (Drs. A. P. Biddle and R. A. C. Wollenberg.)
Fig. 432.—Urticaria pigmentosa (Dr. L. W. Ketron.)

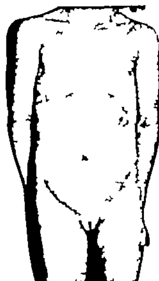


Fig. 433.



Fig. 434.

Fig. 433.—Macula urticaria pigmentosa.
Fig. 434.—Nodular urticaria pigmentosa in 7-month-old boy.

The adult and juvenile types are not distinct, however but are intergradient. Dermographism is limited to the lesions and does not affect the intervening normal skin; this phenomenon is called Darier's sign. Itching may be severe. The trunk seldom escapes involvement, but no region is exempt. Confluence of small yellowish lesions, generalized in distribution and histologically packed with mast cells, gave the patient a pigskin appearance in the unusual case of Graham et al. (ADS 45: 906, 1942). Lymph node enlargement is commonly present. There is no interference with health and well being. The number of lesions is variable sometimes being few or even solitary.

**Etiology and Pathology.**—Little is settled regarding the etiology. The majority of the cases occur in infants. We believe the disturbance a metabolic one, for the patients are in perfect health, excepting their pigmentary urticaria, as most patients with xanthoma seem. Histologically the lesions resemble those of ordinary urticaria, but instead of the usual collection of leucocytes there is usually but not always, an infiltration of mast cells.

**Treatment.**—The disease usually tends to disappear as puberty is reached. Pigmentation in adults is usually enduring. No therapeutic effort is known to be effective.

**Telangiectasia Macularis Eruptiva Perstans** was the title under which Barber and Weber (InternatClin 4: 71 1933) collated cases manifesting telangiectases appearing over the chest, abdomen, and thighs, and showing an interesting interrelationship with urticaria pigmentosa. The eruption consists of discrete small elements which become persisting telangiectases manifesting a brown stain on diascopy. It is our belief that hyperlipemia, especially with lipochrome substances, may damage vessel walls. We have seen "spider nevi" result from overingestion of butterfat, chocolate or cod liver oil and regress after a few months when the diet was altered.

## SEBORRHEA

Seborrhea is a functional disorder manifested by an increase in the amount of the sebaceous secretions. Under normal conditions sebum consists of free fat dry epithelial cells, and epithelial cells which are undergoing fatty degenerative changes. A certain amount of this material is constantly being supplied, serving to protect the integument. Seborrhea may consist in excessive production of either fatty substances or dry epidermic cells. The excess production of oil characteristically gives the skin a shiny greasy appearance. See p. 2[illegible]

**Seborrhea Sicca** is the form characterized by the accumulation of scales or crusts in addition to the abnormal oiliness. This manifestation is doubtless due to infection or malnutrition of the epidermis (see seborrheic dermatitis, p. 332).

**Seborrhea Oleosa.**—This occurs most frequently during the period of adolescence. While the face particularly the nose and forehead, and the scalp are conspicuous sites of the disease other regions are simultaneously involved. This kind of greasiness of the skin, unaccompanied by comedo formation and acne is not responsive to low fat diet and the patients, often red haired, do not tolerate medication with thyroid. The seborrheic tendency is inherited as are likewise the tendency to keloid, xanthoma, acne vulgaris, and premature baldness.

Roentgen therapy, sulfurous astringents, and resorcinol are the most valuable local agents. The skin should be cleansed frequently.

## ROSACEA

**Symptoms.**—Rosacea is a chronic disorder of the nose and face characterized by diffuse inflammation, telangiectasis, seborrhea and acneiform inflammatory lesions. It begins generally on the nose with redness and seborrheic hyperactivity. The process spreads to contiguous areas on the cheeks, involving sometimes the forehead and chin. Crops of acneiform lesions complicate the picture. These are not built about solid comedones, however. They are less acuminate than ordinary acne pustules, and their summits undergo pustulation so as to form comparatively shallow pockets. They may be deeply seated and painful but on resolution leave no scar

In severe cases, the skin is thickened, infiltrated and purplish and the inflammation surrounding separate pustules is confluent.

Keratitis and conjunctivitis are sometimes associated with rosacea. Conjunctivitis may be severe, manifesting small papules of pinhead size surrounded by a ring of dilated capillaries (Low BJD 34 275 1922) Blepharitis also occurs. Iritis accompanying rosacea may occur without corneal involvement. *Vascularization of the cornea may develop* The Negro seems immune to ocular manifestations (Wise AmJOphth 26 391, 1943) Eye changes occurred in only 1.2 per cent of 565 cases reviewed by Marzoni (abs YBD 1948 p 245) Achlorhydria is found in patients with keratitis, according to Johnson and Eckhardt (AOphth 23 899 1940) who obtained excellent therapeutic results in the eyes and erratic improvement of the skin with 3 to 5 mg of riboflavin daily Patients with keratitis reacted positively to testosterone on intradermal testing but not to other hormones, and they could be desensitized, wrote Zondek et al. (BJOphth 31 145 1947) who surmised that these patients were allergic *to endogenous glandular metabolites.*

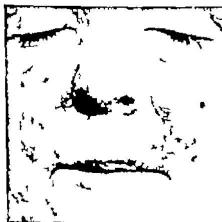


Fig. 435



Fig. 436

Fig. 435.—Rosacea. (Dr W Herbert Brown.)
Fig 436 —Rosacea.

**Etiology** —Rosacea is said to develop as a result of any disorder which gives rise to persistent reflex flushing of the face. The condition is commoner in women. Thyroid and gonadal disturbance, dyspepsia constipation, and overindulgence in alcohol, tea or coffee are associated. Seborrhea, acne, and seborrheic dermatitis are frequently coincident affections *Demodex folliculorum* may play some part in pustulation (Ayres and Anderson ADS 26 89 1932) Gastric subacidity was no more frequently detected in rosacea than in other dermatoses tested by Brown et al. (BJD 47 181 1935) It is our belief that rosacea may represent either of at least two pathologic processes metabolic error involving lipochrome substances, analogous to our interpretation of acne as a pustular lipoidosis and folliculitis dependent on focal infection (see rosacea like folliculitis, p 170) Few cases resembling the rosacea like tuberculid are tuberculous. Some, perhaps those related to *Demodex* respond to 40 per

cent sulfur paste. Some are much benefited by estrogen in balanced dosage others by low fat, low carotinoid diet still others by the administration of riboflavin, pantothenic acid, or other members of the B complex, along with hydrochloric acid Elimination of foci is essential and Vioform ointment is helpful locally in yet other cases. To tell which variety of rosacea the patient has, at the first visit, is a problem which still baffles us.

**Treatment.**—It is traditional to restrict alcohol coffee, tea, pork, sausage, foods rich in shortening highly seasoned or extremely hot or cold foods, cheese, pastries, and nuts. As the main therapeutic measure, Bommer (YBD 1937 p 401) recommended regulation of the diet, utilizing, according to severity and tolerance, diets of (1) fruit, vegetable, and carbohydrate, with a minimum of fat and protein or (2) milk and cream additionally or (3) 300 gm. meat and 2 eggs a week in addition to this. External therapy he regarded as superfluous. Once clear the patient may try prohibited foods, and lesions reappear within 12 hours when an offending one is eaten. We often prescribe a low fat, low carotinoid diet *restricting milk, cream butter ice cream chocolate, nuts, carrot* orange, sweet potato tomato, and egg yolk, especially These women are almost always constipated and often habituated to taking mineral oil from which they must be weaned with the help of a bulky diet and increase in ingested fluids. Riboflavin is promptly effectual in ocular rosacea. Dilute HCl should be given with meals, 1 0 c.c. with water t.i.d., if achlorhydria is present. For external treatment, reliance is placed mainly on sulfur and resorcinol lotions. Telangiectases can be remedied with the electric needle. Refrigeration therapy has been recommended Roentgen therapy is of little value Elimination of focal infection is essential in the management of some cases.

## ACNE VULGARIS

**Comedones** (blackheads) are masses of accumulated sebaceous matter blocking the ducts of oil glands, usually semisolid in consistency and capped at the follicular orifice with a layer of horny débris dark from oxidation. Occasionally the plugs are comparatively hard and can be expressed as firm, oat-grain-shaped, semitranslucent bodies. The face is the commonest site of the lesions, although the concha, the upper dorsal skin of the trunk the sternal region the scrotum, and the shaft of the penis are frequently involved. Exceptionally the lesions may exhibit a tendency to symmetric grouping. They can be expressed and emerge from the follicular orifices as greasy wormlike masses. There may be some associated inflammation. When inflammation is present, it characteristically includes phagocytic leucocytes and foreign body giant cells, *denoting tissue reaction to comedo lipid. This inflammatory* reaction is acne vulgaris. Follicular coccic inflammation resembles foreign body reaction to comedo lipid, for both are furuncle-like in configuration, but they differ in clinical course, cause, and histologic structure

**Acne Vulgaris** is a chronic inflammatory disorder involving the sebaceous glands, characterized by the development of shallow or deep pustules and abscesses built about and intermingled with comedones. The face is the site of predilection although the sternal region *shoulders*, and back may be attacked Lesions may occur wherever comedones may be found The eruption is symmetric as a rule It is usually limited to areas in which sebaceous glands are normally plentiful and well developed; but



Fig. 537



Fig. 538.

Fig. 537.—Acne vulgaris. (Drs. Fordyce and MacKee.)
Fig. 538.—Scarring from acne. (Drs. I. R. Pels and J. W. Lord.)





Figs. 539 and 540.—Acné excoriée, a form of neurotic excoriation.



Figs. 541 and 542.—Acne lgaris, chronic nd severa. (Dr H. C. Varney.)



Fig. 543.—Acne lgaris.



Fig. 544.—Comedo in f t gland duct.

the scalp is not involved excepting occasionally at the occiput, where acne may be manifested as folliculitis keloidalis. The sebaceous glands associated with lanugo hair are the ones principally affected. The lesions usually develop rapidly and in crops, and each persists for several days or weeks. While acne papules and pustules may occur on dry skins, oily seborrhea is generally a conspicuous concomitant the integument appearing relaxed, dark, and greasy

Acne nodules, pustules, and cysts seem histologically to be foreign body granulomas with leucocytes phagocytes, and giant cells. The process may affect the superficial part of the sebaceous apparatus, so that small acuminate pustules are seen; or deeply seated oil depots may be involved, so that the clinical lesion is a deep, tender reddish, sluggish nodule. Deep lesions may become cystic. By extension and coalescence, they may involve the conjoined deep portions of several sebaceous glands so as to form painful, boggy tumors Intergradient types of lesions may occur in the same individual. Hyperkeratosis of the follicular orifice is a recognized feature of comedo formation (Sulzberger et al.: NYSJM 34; 899 1934) and perhaps this results in the accumulation of fat in the follicle In inflammatory lesions, Lynch (ADS 4. 393 1940) found fat mainly in epithelial cells or in dead epithelium, but he did not attribute the inflammation to the lipid, as we do. The studies of Ham (APath 26 936, 1152, 1166 1938) of tissue reactions to fatty substances are interesting and pertinent.

Superficial lesions are likely to rupture so as to discharge a more or less solid comedo or the liquid fat representative of it along with creamy pus. Deep indurated nodules may eventually discharge or their soft, greasy purulent material may undergo organization and heal or the contents are phagocytized and carried away or else become encysted by epithelium so that a sebaceous cyst forms or the contents are taken up by histiocytes and firm, xanthoma like nodules result, and these resorb only after many months have passed What the patient does to the lesions is an additional variable factor and neurotic excoriation may exceed the disfigurement due to acne itself

Scarring varies greatly in different individuals. Superficial lesions give rise to little scarring but a full-blown lesion results in sloughing out a sebaceous gland so as to leave a pitted scar When lesions are deeply seated abscesses, there ensues more or less destruction with resultant scar formation. In the course of years, disfigurement lessens, but it is permanent Undermining and coalescence of the pathologic process affecting nearby follicles results in honeycomb lesions and bridge scars.

**Clinical Variants.**—**Acne Papulosa** is the type in which there are many comedones and some papular inflammatory lesions. **Acne Pustulosa** is comparatively superficial but pustular **Acne Indurata** is deeply seated, perhaps secondarily infected. **Acne Cystica** may be manifested with only a few or perhaps many deep, cystic lesions containing gelatinous pus. **Acne Cachecticorum** is characterized by large soft, purulent, ulcerative cystic and scarring lesions. In **Acne Atrophica** comedones and pustules disappear leaving a retiform pitting and scarring like folliculitis ulerythematosa reticulata (p. 5 ..) **Acne Conglobata** is severe acne with multiplex comedones which are confluent beneath the follicular orifices and productive of large cystic lesions and bridge scarring. It may be limited to axillary or perianal distribution and so comprise one variety of hidradenitis suppurativa (Pulton and Marks J L.1 1344 1943; Marks KSLJ 39 477 1946) **Infantile Acne** occurs in the extremely young especially when the nourishment includes too much cream or codliver oil (Aitken BJD 55 272, 1943) A nursing baby with acne had been born with pustules, and its mother had received bromides, reported Goldsmith (BJD 57 135 1945) **Miliary Acne** manifests numerous pinpoint to pinhead size superficial, but ... (Thompson and Kocherman MRec 159 670, 1945) **Tropical Acne** affects the back especially develops and disfigures rapidly in persons of a slightly older age group and is apparently caused by hot wet climate (Kovy CalifM 63 ..4, 1946 Trans A.D.A. 1947; Sulzberger et al.: USNMBull 46 1178, 1946) **Acne Cheloidalis** is the type in which keloids evolve about the large

deep comedones, pustulation being comparatively mild and the lipoidal foreign substance becoming encased in dense fibrotic tissue. **Acné Excoriée** is the diagnosis when there are little acne and much neurotic excoriation.

***Symptomatic Acne (Acne Artificialis)*** *develops from extrinsic causes.* Bromide and iodide rashes resemble acne (Sulzberger et al.: NYSJM 34: 899 1934). Iodized salt has been alleged as a cause as has bromine vapor. Occlusion of the follicular orifices by oils or paraffin is an etiologic factor and is often seen among workers in binding twine factories (Mavers and Silverberg: JIndustHyg 20: 244, 1938); see Oil Acne (p. 82). Viosterol and halibut oil may cause eruptions of small acneic lesions (Pfister J 102 633, 1934). Masculinizing adrenal tumors often provoke acne (Kepler et al.: PSMMC 13 353 1938) as may injections of androgen (Hamilton JCIEndocr 1: 5 0 1941).



Fig. 445.

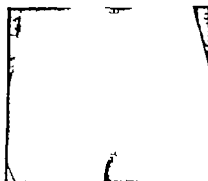


Fig. 446.

Fig. 445.—Acne of shoulders and back.
Fig. 446.—Chloracne. (Dr W. M. Howell.)

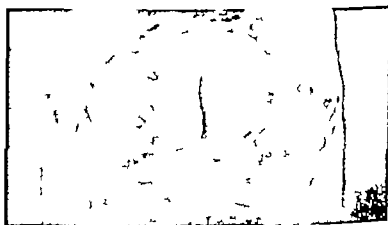


Fig. 447.—Acne conglobata. (Dr F. Ronchese.)

**Prognosis.**—Acne vulgaris is an obstinate and spontaneously scarring disorder prone to relapse and to recur. Perseverance in good treatment is usually followed by acceptable improvement, however and this disease, typically of adolescence, sometimes disappears spontaneously as the years go by. Niles (ADS 27 89 1933) indicated that the amount of scarring in acne vulgaris is largely dependent upon the severity and dura

tion of the disease and is neither increased nor decreased by roentgen therapy Treatment which prevents the development of new lesions and which curtails the suppuration of inflammatory ones, is best. Evacuation of pustules, if properly done, lessens the scars which might be expected.

**Etiology and Pathology**.—Comedones may occur at any age, but they usually develop during the adolescent period. Factors in the production of comedones are disturbances which tend to increase the activity of the sebaceous glands. Greasy-skinned individuals of the so-called seborrheal type are predisposed The epidemiologic study of Hinrichsen and Ivy (ADS 37 975 1938) showed no sex preference but acne appears a little earlier in girls in association seemingly with their earlier sex maturation. The incidence diminishes in men after age 19 but clinical acne is common even after age 30 (Forbes BJD 58 298 1946) This is true also of women (Cohen BJD 57 10 1945) Constipation dyspepsia, fatigability anemia, and menstrual derangements are frequent concomitants these are also symptoms of hypothyroidism, a disease characterized by hyper lipemia. Heredity is responsible for a predisposition to acne (Hellier BJD 51 109 1939)



Fig. 312.—Acne vulgaris, histologic lesion. Leucocytic, phagocytic, and giant cell infiltration in and about sebaceous gland. Arrector pili at upper left.

*Corynebacterium acnes* is thought by some to be the exciting cause of acne but no one ever caught acne, and pus from the lesions is innocuous. Vaccines of *C acnes* are worthless (Costello and Washburn ADS 38: 45, 1938) Exacerbations occur during intercurrent illnesses and often at the time of menstruation. Iodides make acne worse. The blood iodine levels of acne patients does not differ from controls (Traub and Emmet ADS 41 506, 1940)

**Nutritional Considerations**.—On a high carbohydrate diet 10 patients in hospital became better not worse Crawford and Swartz (ADS 33: 1035, 1936) reported. White (J 103: 1277 1934) and Cormia (JAllergy 1.: 34 1940) knew that some acneform eruptions depend on foods and can be cured by elimination diets, and that they are not distinguishable by skin tests In avitaminosis A (p. 430) there is a supplanting of follicular and glandular epithelium by keratinizing squamous epithelium, so that follicles become plugged, secretion is diminished and the skin is dry Acne appears in vitaminosis A with noteworthy rarity (Lowenthal ADS 28 700 1933) but acne can be caused by taking fish oils to excess Thyroid function is necessary for the metabolism of fat (Hurxthal AI tM 53 762, 1934) and in hypothyroidism, hyperlipemia is present. Milk, cream, ice cream, meat and chocolate are the commonest fat rich foods, and they cause comedones and acne when ingested in amounts beyond a person's metabolic capacity The balance between the the intake of lipid and its management when absorbed, dependent as its metabolism is on endocrine function, especially thyroid, is the balance which determines seborrhea and the formation of comedones we think

(BMJ 84 1071 1941) Cholesteremia is not concerned (Strickler and Adams ADS 26: 11, 1932 Lewinn and Zugerman: JLCM 28: 190 1942) but no one has studied total and fractional blood lipids quantitatively in acne.

When the acne patient on a low fat diet drinks milk, new lesions appear in about 36 hours, the time required for fat to be deposited and tuberculoid inflammation to develop. Lipochrome pigments are significant as well, for catsup and excessive orange juice have as bad effects as butterfat. Menagh et al. (JMichMS 37: 5.1 1938) found diminished carbohydrate tolerances in 70 per cent of their cases and reduced B.M.R.'s in 63 per cent they gave insulin to the one group and thyroid to the other with beneficial effects for the most part but they disregarded diets.

Endocrine Influences.—The age of onset is coincidental with sex maturation, and is somewhat earlier in girls. Acne is a young person's d ease, is a d hormonal dermatosis, and shows predilection for thick skinned persons of dark pigmentation (Bloch BJD 43: 61 1931) Many studies have been concerned with attempts to control acne vulgaris by the use of various hormonal substances. Without reviewing them in detail here we believe it fair to say that the results have been irregular unsatisfactory and unpredictable. See also Cohen (BJD 53 231 269 1941)

An oversupply of male sex hormone may be concerned (Wile et al.: ADS 39 195 1939) although increase or diminution of androgen excretion has not been proved in either sex. Laurence and Werthessen (Endocr 27: 733, 1940) did report a disturbance of androgen-estrogen ratio Cohen found no support for a hypothesis that psychiatric factors are involved in the causation of acne (BJD 57: 45, 1943) he observed no significant relationship between seborrhea, dandruff and acne (Ib. 57: 43, 1943) there was no association with hypertrichosis (Ib. 5 102, 1944); but heavy sleeping and the lack of feeling refreshed by sleep occurred in patients of both sexes (Ib 57 14 1943) confirming an bservation of ours of symptoms we attribute to hypothyroidism for they disappear when the correct dose f thyroid I established.

**Treatment.**—The patient is carefully instructed to avoid traumatizing the face, which should be washed gently with soap and to which no unguent may be applied Petrolatum on the hair gets on the face Seborrheic dermatitis of the face dry skin, is simply the extension of dandruff of the scalp which should be treated (see p 332) Authorities differ in their ways of trying to cure acne, *there being recognized no one best way* (JInvD 3 143 1940)

Local Treatment of the comedones and pustules is delicate and exacting minuscule surgery which must be performed by the physician the patient being prohibited from picking at his lesions. The purpose of local treatment is to get rid of lipid depots before they provoke inflammation or with as little trauma as possible after they have done so Traditionally one *prescribes a sulfurous astringent such as lotio alba*

| | | |
|---|---|---|
| ℞ | Phenol | 1.0 |
| | Zinc sulfate | [illegible] |
| | Sulfur pptd. | |
| | Sulfurated potash | [illegible]0 |
| | Rose water | 180.0 |

A complex sulfur preparation in a penetrant wetting agent vehicle (MacKee et al JInvD 6 309 1945) has been *highly recommended.*

To peel the face with a powerful agent may be undertaken only under closest supervision it is dangerous and violent and does not have lasting beneficial effects (Eller and Wolff J 116 934 1941 QMN J 122 1277 1943) Ultraviolet light is temporarily helpful in mildly peeling dosage Cryotherapy popular impressive and temporarily beneficial through its peeling effect (Karp ADS 39 995 1939) is accomplished by grinding solid CO in a mortar with acetone to make a slush, which is quickly swabbed over the affected parts (Dobes and Keil ADS 42 547 1940)

Its defatting and exfoliating influences are creditable, but its value in amelioration of scars is at best dubious (Friedlander ADS 46 734, 1942) Zugerman (ADS 54 200 1946) used ethyl acetate as the vehicle and added sulfur to the refrigerant. The technic of peeling the skin was given by Urkov (IllMJ 89 75 1946) but our citation is not a recommendation.

ROENTGEN THERAPY produces necrobiosis and atrophy of sebaceous follicles, but does not influence the cause of sebaceous hyperactivity Roentgen therapy will not rid the dermis of embedded comedones and waxy cysts, which must be removed mechanically It may be relied upon to improve a higher proportion of patients than any other single agent (King and Hamilton JTennMA 34 272, 1941 Smith Texas SJM 38 512, 1942) It is generally not advised for patients under 16 years of age Given on only one side of the face it seemed to Kline and Gahan (ADS 46 207 1942) to help both sides. It is not the sole agency for treatment (Twining PaMJ 44 1165 1941) but works especially effectively in conjunction with low fat diet and thyroid therapy Cole and Driver told us. Exacerbation may follow its use in cystic cases. MacKee recommended doses of 75 r each week at 80 to 100 kv most patients will tolerate 3 or 4 months of this without atrophy he stated, but after 4 months one must stop Fair and pustular patients may tolerate only half as much The danger of resultant permanent injury must be continually borne in mind.

GENERAL MEASURES.—One should discourage free sweating for to sweat is to secrete also an increased quantity of sebum. Adequate sleep is desirable for chronic fatigue is certainly a harmful influence. Sexual tension is undesirable but is often unavoidable We see acne disappear after marriage and see it reappear along with neurotic excoriation after divorce.

Focal infections must be eliminated in some instances, for tonsillectomy may work wonders in a severe and difficult case.

Tonics may be employed, such as the venerable I.Q and S., or the more modern B complex pill Marshall (JInvD 2 205 1939) recommended a liver extract Riboflavin useful in rosacea, may help here. Viosterol in doses of 20 000 to 100 000 units daily has been followed by improvement in many patients and harm in few (Maynard ADS 41 842, 1940) Large doses of vitamin A were recommended by Straumford (NoWM 42 219 1943) but Lynch and Cook (ADS 56 356 1947) were unable to confirm him. Acne is not a vitamin problem, but when vitamins are needed in any condition their administration is helpful.

Penicillin by injection benefits secondarily infected and painful acne it can at best only subtract the infectious fraction of the patient s disease Foreign protein therapy has largely been relegated to history

ENDOCRINE THERAPY —There is no question that hormone imbalance plays an important etiologic role but how much of which hormones to give under what circumstances are difficult questions. There is growing belief that estrogenic substances are helpful in some cases of acne. In the severe cystic type in males, we have followed the recommendation of Belbario to give 1 mg of stilbestrol daily for a week or two in a course desisting when the nipples become sore and we think benefit has accrued The natural estrogen in aqueous suspension given during the first three weeks of the cycle in modest dosage has helped the skin as well as the abnormalities of menstruation in some of our acneic girls, especially those whom thyroid has not helped We are not as yet prepared to give depend-

able rules for the administration of estrogenic hormones in this disease. We are convinced of the value of thyroid however in the large majority of the patients.

DIET AND THYROXIN —Taking into account the noninfectious nature of the disorder the greasiness of the skin and the evidence that senile inflammation is tissue reaction to lipid, we hold it advisable (JKansMA 48 545 1947) to see that the patient does not take much oil in through his mouth so that he cannot put much out through his skin. We prescribe therefore, a low fat diet which may contain as many calories as the patient can swallow. If he ingests fewer calories than he consumes, he loses weight, for the calories he burns but has not ingested must come from his own stores of fat. Therefore a diet on which the patient loses weight is not a low fat diet, and patients losing weight do not show improvement. To accomplish low fat nutrition the patient must be on a high protein, high carbohydrate diet. In designing the diet, the tables of Chatfield and Adams, U S Dept. of Agriculture Circ. No 549 are useful. In general foods of vegetable origin are low in lipid content, and foods of animal origin are oily

LOW FAT DIET

General Instructions.—A diet to be followed for a long time must be adequately nutritious, easy to follow and fit to eat. There is no restriction of quantity eaten. *Do not go hungry* Keep a record of weight. This is not a diet for allergy wherein 100 per cent of certain items are interdicted. Restrict does not mean not any of

Allow —Fruits, cereals, bread, vegetables, sugar and sugary foods (such as syrup honey jelly and sugar candy) lean meats, birds, game fishes, gelatin, cottage cheese, egg white.

Restrict.—Milk (do not drink it) cream, butter (1 square per meal is all right) ice cream, cheese (like butter) gravy and salad dressings (a teaspoonful makes foods more palatable, is allowed) ham, pork, fried foods (potato chips are 35 per cent oil by weight), popcorn and substances rich in lipochromes, which are not successfully metabolized by acneic individuals, such as tomato catsup and juice, carrot, cereal e egg yolk and orange juice, and cod liver oil.

THYROID EXTRACT enhances lipid metabolism and regularly lowers lipemia. We consider the correct utilization of thyroid to be that of a normal person, in whom any additional thyroid is too much. We seek to dose the acne patient so that he resembles the normal in that more thyroid would be too much The correct dose is found by experiment placing the patient on 1 gram U S.P with breakfast each morning it is easy to discover whether this dose is too little and does nothing too much and poisons the patient however mildly or is just right. We are like perhaps half of all internists in disregarding the B M.R in which we have neither confidence nor interest We sometimes give regard to the basal temperature obtained by holding an accurate thermometer in the mouth for 5 minutes prior to arising and reading it to the tenth of a degree A temperature below 97 8 F suggests that thyroid may be increased a trifle but at 98.2 F overdosage symptoms are present or imminent (Barnes J 119 1072, 1942) The maximum tolerated dosage is *just less than* that which produces any symptom of overdosage

Symptoms of overdosage include nervous tension, insomnia and restlessness, headache dizziness, weakness, tremor palpitation, and continued loss of weight Milk is the antidote for thyroid overdosage as sugar is for insulin At the *first* appearance of any symptom of intolerance the dose is diminished to a tolerated level This necessitates keep-

ing the patient under strict supervision, seeing him each week, recording his weight inquiring of him how he tolerates the medication and making suitable adjustments of dosage.

Correctly administered this regimen of diet and thyroid substance cannot be harmful for enough vitamin A leaks into the diet to prevent hypovitaminosis. As soon as a proper level of thyroid intake is established, seborrhea and inflammation greatly diminish. The diet is strict at first and is broadened as the disease is controlled until the patient discovers how much fatty food he can ingest without erupting

SUMMARY.—In addition to diet and thyroid, we make use of painstaking surgery x ray therapy after the correct dose of thyroid is established, such measures as attention to focal infection and administration of penicillin if they are indicated, and no local medication at all.

## CUTANEOUS SYMPTOMS OF ENDOCRINE DISEASES

**Addison's Disease.**—Atrophy dysplasia, calcifying tuberculosis or other destructive alteration of the adrenal glands results in disease usually of insidious onset, early manifested by asthenia and dizziness on change of posture. Anorexia and nausea f llow; later irregular crises occur with collapse, dehydration, hypoglycemia, and hypotension, and death is imminent in these. Melanin pigmentation of skin and mucosae is common, may appear early but is not necessarily present. Its intensity ranges from light to almost black. It is diffuse but is deeper on exposed parts and intensifies normal pigmentation. The neck, flexures, and regions affected by acanthosis nigricans are the sites of predilection. Over the diffusely pigmented skin there may be little mole like spots of deeper pigmentation, and upon the trunk, particularly on the lower abdomen, it may be "ribbed" like the sand on the seashore (Osler and McCrae: Medicine Appleton) The mechanism of the pigmentation is obscure.

ADRENAL CORTICAL INSUFFICIENCY is recognized by the characteristic changes in the clinical picture and diagnostic blood chemical findings of high urea and potassium and low chloride and sugar (Sigland PSIMIC 22: 17 1947) "The patient is perched on the brink of a physiologic volcano (Conference on Therapy J 112 2311, 1939) Diagnosis of crisis is suggested by marked prostration, hypotension, hiccups, and signs of circulatory collapse. The 24-hour urinary excretion f 17 ketosteroids is diminished; the finding of more than 4 mg in women or 10 mg in men tends t exclude Addison's disease as the diagnosis. Restriction of sodium chloride intake provokes indications f adrenal sufficiency and, while a dangerous procedure, this may be performed for diagnosis (Cutler et al. J 111 117 1938 Willson et al.: AIntM 69: 400 194.) When the adrenal cortex is deficient, it cannot of course, respond to stimulation by purified pituitary adrenocorticotropic hormone when the drenal cortical reserve is adequate, the injection of 25 mg. of the pituitary hormone is followed by a decrease of 50 per cent or more in the urinary uric acid creatinine ratio (Thorn et al. J 137 1005, 1948) Such a decrease does not occur in Addison disease.

TREATMENT with high salt, low potassium diet and desoxycorticosterone acetate starting with 50 mg subcutaneously per day is effective (Thorn and Firor J 114 2517 1940) Pellets of the steroid may be implanted under the skin so that gradual absorption meets the patient's need (Thorn et al BullJHH 64 339 1939 Engel et al.: AnnIntM 17: 683, 1943) Transplantation of adrenal tissue from another person may have cured a patient (Broster: BMJ 2 750, 1946) With successful treatment, pigmentation may diminish or disappear

The chemical similarities of sex hormones, desoxycorticosterone and related substances of notable physiologic activity were interestingly presented by Mason (PSMMC 15 289 1940)

**Acanthosis Nigricans** a disease f chromaffin tissue insufficiency The cutaneous manifestations comprise melanin hyperpigmentation and papillomatous hypertrophy affecting the axillae neck, genitalia and groins, face, medial thigh, antecubital and popliteal regions, and about the umbilicus and anus. Constitutional symptoms include asthenia, hypopiesis, loss f weight, anorexia, hypometabolism, decreased 17 ketosteroid excretion, and diminished serum sodium and chloride concentration, as in Addison's disease (Thorn J 125 10 1944) Juvenile and adult cases may be distinguished, the juvenile being usually benign in etiology and the adult depending generally on tuberculous or neoplastic destruction of the adrenal and retroperitoneal

chromaffin tissues. Some juvenile cases are associated with obesity, which is usually of the pituitary type (Robinson and Tasker: ADS 55: 740 1947) Curth (ABurg 47: 517 1943) reported benign and malignant cases entirely similar insofar as skin changes are concerned. Half of the cases are cancerous in origin and over 90 per cent of the cancers are abdominal, usually gastric, glandular and highly malignant. Skin changes have been known to precede the recognition of cancer by 6 years. They sometimes



Fig. 549.—Acanthosis nigricans. (Dr Wm Frick.)

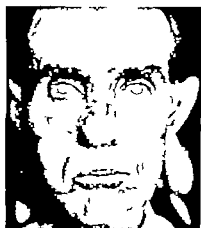




Fig. 550 Fig. 551

Fig. 550.—Acanthosis nigricans.
Fig. 551.—Acanthosis nigricans. (Dr Stuart W y.)

regress when the cancer is treated and relapse when it recurs. The benign type usually appears before or during puberty. Familial cases occur and these are usually benign. The spread of skin changes after puberty is a bad omen. The skin lesions are usually symmetric in malignant cases and when asymmetric, which is rare, the case is usually benign.

The disease is comparatively rare. Cutaneous lesions may develop slowly and insidiously or rapidly. The flexures and the face, lips, mouth, and nipples are the sites

of predilection, although no region is exempt. The earliest manifestation is usually hyperpigmentation, the affected skin assuming a reddish, brownish or blackish hue which gradually fades off at the margin. The epidermis becomes thickened, but without accompanying induration, and the natural lines of the skin are exaggerated. These changes are followed by the development of numerous soft, millet seed to pea-sized, papillary growths. These little tumors are often accompanied by crops of warty papules which are distributed irregularly over the hands, forearms, and thighs. There is generally more or less associated hair loss, particularly of the scalp and eyebrows, and the nails usually become striated and brittle. Hyperkeratosis of the palms and soles is a common accompaniment. The buccal mucosa may be thickened and velvety or granular in appearance, or it may be the site of numerous small, papillomatous growths. The natural course of the disease is usually progressively downward, with acute exacerbations at irregular intervals. Spontaneous remissions may occur. An occasional patient seems to recover. Only the absence of papules and verrucous lesions differentiates Addison's disease from acanthosis nigricans. Eleven cases each of the benign juvenile and malignant types were reviewed by Kierland (JInvD 9: 299 1947), who noted that the histologic features of early acanthosis nigricans resemble those of normal axillary skin.

Supportive measures and rest are indicated. Various extracts of adrenal cortex have proved successful in replacing the deficiency as in Addison's disease q.v. In a crisis, cortical extract alone is not sufficient; sodium chloride must be given. See Pollitzer (J 53: 1869 1909) McCullagh and Ryan (J 114: 2530, 1940); see also p. 2517 and p. 2526)

**Acromegaly** due to pituitary dysfunction with excessive production of growth stimulating hormone by the eosinophilic anterior lobe cells, is characterized by hypertrophy of the bones and soft parts, particularly of the face and the extremities. The onset of the disease is insidious, and its course progressive. The parts affected by predilection are the face particularly the lower jaw the malar bones, the supraorbital prominences, and the *distal ends of the extremities*, although no region is *exempt*. Cutaneous changes include thickening, coarse and wiry hypertrichosis, and often areas of pigmentation. Epidermal, glandular and collagenous hypertrophy and pigmentation of the rete are found (Simpson: BMJ 2 931, 1930). Enlargement of fingers and toes, furrowing of the forehead skin and periostitis, without elongation of bones, typical skull or jaw changes or cessation of progress after age 25, were described as acropachyderma with pachyperiostitis by Brugsch (AIntM 68 657 1941).

**Hyperthyroidism.**—The blood lipid is low and the administration of iodine or thyroidectomy results in rise of the cholesterol level (Man et al.: JClinInv 19 43, 1940). The skin is warm, flushed, moist, and *free from acne*. The hair *tends to be thin* and of fine texture and the nails thin and fragile. In Graves' disease perspiration and flushing may be complaints; pruritus is sometimes annoying; multiple telangiectases have been described and pigmentary changes, patchy or generalized, may be seen.

**Myxedema** is due to extreme thyroid insufficiency. The onset is usually gradual, with anemia, weariness, depression, irritability, mental listlessness and characteristic cutaneous changes. The skin becomes dry, rough, yellowish, and swollen and does not pit on pressure. There is more or less dandruffy scaliness, and sweat secretion is diminished. The cutaneous regions commonly affected are the face, particularly the lips, nose and eyelids and the neck and hands. The swollen, masklike *face, everted lips*, expressionless eyes and pudgy hands combine in an appearance which is distinctive. Volar hyperkeratosis is a common symptom.

MILD DEGREES OF HYPOTHYROIDISM are common, and in adolescents the condition is often associated with acne (p. 403). Hypothyroidism interferes with metabolism of lipoids including vitamin A. Cutaneous lesions comprise only a part of the widely distributed myxedematous changes. The B.M.R. may or may not be lower than normal (Mason: BMJ 36 309 1939). The patient may be fat or thin, and the thin hypothyroid child may be nervous and hyperkinetic (Rose: PaMJ 42 732, 1939). Anemia, constipation, menstrual disorder usually in the form of delay and scantiness *occasionally* with excessive flow, and sterility are among the symptoms. Lack of energy drowsiness and failure to be refreshed by sleep are typical (Kimball: KyMJ 31 498, 1933). The diagnostic criterion is the response to thyroid therapy (Wilkins: J 114 2382, 1940). Blood fat is affected, the hypothyroid being hyperlipemic (Boyd and Connell: QJM 6 467 1937); but cholesterol may be normal while total lipid is significantly elevated (Rudwin et al.: AmJDisChild 60 1120, 1940).

Administration of thyroid causes blood fat concentration to diminish toward normal; overdosage causes diminution to subnormal levels.

**Circumscribed Myxedema.**—Pillsbury and Stokes (ADS 24: 233, 1931) recognized types: those with nodular papular or diffusely infiltrative lesions distributed



Fig. 552.



Fig. 553.

Fig. 552.—Acromegaly. (Meakins' *Practice of Medicine*, Mosby Co.)
Fig. 553.—Myxedema. (Meakins' *Practice of Medicine*, Mosby Co.)

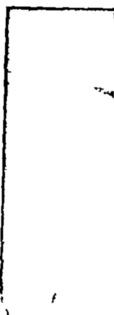


Fig. 554.



Fig. 555.

Fig. 554.—Localized myxedema. (Dr. [illegible] Sweitzer.)
Fig. 555.—Keratoderma climactericum (Haxthausen). (Dr. O. G. Costa.)

on the face, arms, back, and scrotum; and those with similar lesions on the shins. The disseminated type may respond to thyroid medication; the commoner pretibial type does not. The 6 cases of O'Leary (ADS 21: 57 1930) were associated with hyperthyroidism, as is usual, and with chronic edema of cardiac decompensation the lesions were nonpitting, tawny plaques on the legs. Numerous cases have been described (Schwartz and Madden ADS 43 375 1941, Becker and Rothman: ib. 46: 831, 1942; Netherton ib. 48: 123, 1943; Cohen: BJD 58: 173, 1946, with bibliography) Histologically one finds mucous infiltration of the cutis and immature connective tissue cells, or star cells. The cause is unknown and treatment is unsatisfactory it being unusual for the lesions to disappear even when the presumably etiologic toxic thyroid is removed (Handley and Downing ADS 40: 374 1939)

**Dermatitis Dysmenorrhoica** is a peculiar dermatosis which occurs rarely in women having dysmenorrhea, manifesting itself during the menstrual periods and at no other time. The eruptions consist of usually symmetric lesions affecting the face, trunk, and extremities, appearing in the form of erythematous patches, urticarial wheals, or, more often, vesicular eruptions resembling eczematous dermatitis (Urbach: InternatClin 2: 1939) Blood serum obtained during an urticarial flare and readministered to the patient in the intermenstruum caused reappearance of urticaria but did not affect controls (Harrison: J 100: 738, 1933) Not all cyclic rashes of menstrual periodicity are dyshormonal. Repair of cervical erosions, endometritis or cystitis due to cystocele may rid a woman of focal infection and dermatitis secondary thereto Yet some cases of rosacea respond at once to suitable doses of estrogen and to no other medical effort.

**Endocrine Keratoderma.**—Keratoderma climactericum was the title given by Haxthausen (BJD 46 161, 1934) to a usually asymptomatic affection characterized by the occurrence of circumscribed hyperkeratoses f the palms and soles of obese and hyperplastic women at the menopause, who may have arthritic symptoms also. Hypothyroidism underlies the development of volar hyperkeratoses in certain instances (Cervino et al. Endocr 22 615 1938) Goldberg (ADS 40: 67 1939) cured his case by injections f 2,000 units of estrogen in oil twice a week. Lynch (ADS 48: 270 1943) described the commencement of the disturbance with sharply circumscribed oval papules which progress become scaly and eventually coalesce, after which fissures may appear and secondary infection may develop. His histologic studies revealed mainly hyperkeratosis with some swelling and degeneration of elastic and collagenous tissues and mild lymphocytic inflammation. The patients of Garbe (ADS 49 254, 1944) responded well to estrogen but relapsed when it was discontinued.

**Diabetes Mellitus.**—Cutaneous manifestations include those due to dehydration and to dysfunction of metabolism f vitamin A and carotenoid pigments (p. 394) Eruptive xanthoma (p. 385) and necrobiosis lipoidica (p. 390) have been described. Lamb and Kaltz (OklaSMAJ 34 93 1941) reviewed these conditions and discussed also pruritus, which may be generalized or localized to the genital region, insulin allergy (dermatitis medicamentosa, p. 107) and susceptibility to tinea, secondary infection, furuncles and gangrene (pp. 165, 183)

**Diabetes of the Skin** was postulated by Urbach (J 129 438, 1945) in a patient whose intracutaneous sugar concentration seemed not to parallel that of his blood, an independent cutaneous glycohistechia. The clinical picture was of furunculosis, sweat gland abscesses, eczema, and pruritus, responsive to low carbohydrate diet with or without insulin. Submitted as proof was a solitary point on the dotted line representing the skin sugar content t the third hour in his chart 1.

**Pregnancy.**—Symptomatic eruptions in pregnancy were reviewed by Costello (NYSJM 41: 849 1941) who listed the etiologic factors as endocrine, toxic, and neurogenic. Urticaria, dermographia, generalized pruritus, pruritus vulvae, prurigo, *herpes gestationis*, *impetigo herpetiformis*, *molluscum fibrosum gravidarum*, pigmentation, edema, hyperhidrosis, volar telangiectasia, and hypertrichosis were noted

**Diabetes Insipidus.**—Mild pruritus, dry skin, xerostomia, and lack of sensible perspiration were described by Brayton (J 43 377 1904)

**Pituitary Basophilism.**—Cushing (BullJHH 50 137 1932) distinguished a group of cases in which physiology is altered because of basophile adenoma f the pituitary gland so that there occur obesity amenorrhea, weakness, hypertension, albuminuria, lowered sugar tolerance, kyphosis, and bone pains. Notable dermatologic changes have accompanied the foregoing manifestations. Striae distensae may reach a remarkable development. Purpura and ecchymoses are common. Hypertrichosis of the face and trunk is usual. Freyberg et al. (AIntM 58 187 213 229 1936) urged intensive radiation of the pituitary gland as the only useful therapeutic measure. The syndrome may rise from suprarenal lesions as well as pituitary

## GOUT

Gout is characterized by the deposition of urates, chiefly the biurate of sodium, in and about the tissues of joints, particularly the cartilages, most frequently affecting the metatarsophalangeal joint of the great toe the knee joint, and joints of the fingers. Urates are deposited also in the soft tissues of the joints, in the eyelids, in the cartilages of the ear and in the subcutaneous tissues, especially of the hands. Tophi are nodules of considerable size and over them the skin may ulcerate so that there occurs discharge of hard chalklike masses, followed by temporary healing. Urates do not obstruct the x rays more than soft tissues do.

Exacerbations are acutely painful. They are preventable by adherence to a low purine diet (Hench: J 116 453 1941) which allows milk, eggs, cheese, caviar, shad roe nuts gelatin, sugar sweets, tea, coffee, cocoa, fats of all kinds, fruit of all kinds cereals excepting whole grains, bread excepting whole grains, vegetable soup without meat and vegetables of all kinds *excepting* lentils, spinach, mushrooms, peas, lima beans, navy beans, kidney beans, kohlrabi, asparagus, and onions. Foods rich in purines include sweet breads liver kidney squab, tongue, turkey pork, veal, sausage beef goose ancho ies sardines, trout, pike perch, codfish, lentils, gravies, meat extractives, and meat soups. All wines and liquors should be avoided.

The intermittent use of cinchophen is almost always necessary. A method of dosage recommended by Graham (ProcRoySocM 1 1 1937) i 0.5 gm. t.i.d. for 3 or 4 consecutive days each week for several weeks. During the taking of cinchophen, the patient should ingest also a quart or more of water a day and maintain alkalinity of the urine with sodium bicarbonate, 2 teaspoonfuls in the morning and one in the evening. Early signs of intolerance of cinchophen are nausea, hives or other skin reactions, and urobilinogenuria. On the appearance of such symptoms, the drug *must be stopped.*

Surgical removal of tophi relieves pain (Linton and Talbott: AnnSurg 11 161 1943)

Volar erythema with hyperkeratosis at pressure points, itching and burning with or without painful fissures may improve on antigout therapy (Barber: ProcRoySocM 31: 701 1938)

## HEMOCHROMATOSIS

Hemochromatosis (Hemosiderosis Bronze diabetes) is a rare disease characterized by the deposition of large amounts of hemosiderin in glandular tissues and hemofuscin in the connecti e tissues, spleen, and smooth muscles. The onset is usually after the age of 35 years. Pigmentation and cirrhosis of the liver and pancreas with impotence diabetes ascites and terminal jaundice are the typical features. Pedigree studies suggest that this inborn metabolic error is transmitted through the female (Lawrence Lancet 1033, 1935) Iron is increased in qua tity in all the tissues excepting the blood bra n, and colon, and there may be relatively enormous amount in the li er pancreas, l mph nodes, thyroid pituitary salivary glands, *choroid plexus,* and heart. Butt and Wilder (APath 26 262, 1938) observed that of 30 known cases, 29 were males. The bronze skin is of a hue between that of Addison disease and of argyria.

Th sk n bi psy usually show ron-containing p gment in the propria of the sweat gland and superficial capill ries of the cutis. Th ntracutaneous injection f 0.5 pe cent potassium ferrocyanide in 0.01 normal HCl yields a blue color diagnostic of the presence of ron (F shba k JLCM 3 98 1930)

Asthenia is a frequent complaint. Regression of seconda lary sex characters is a symptom, with pallor nd loss of axillary pubic and beard ha (Fepler et al. AnnIntM 14 810 1940) The colo changes i the ski are ot invariably present and may appear early or late the course f the disease. Differentiation from Addison s disease and from argyria is read l made by noting the hanges in the urine. The cirrhotic l er i smooth and firm but not very hard. The patient does f irly well if the diabetes is ntrolled, but in the late stages thi s d ficult to do. A high protein, high carbohydrat diet is recommended (Bloom A MMonth 66 79 1930)

## OCHRONOSIS

Ochronosis is the name suggested by V rchow (Arpath Anat 3 1 1866) for a rare disorder chara terized by gray h browni h or bla ki h pigmentation of the cartilages, ligament tendons and intima of the large blood vessels. I addition t the deposits in the int rnal tructures, the p gment is frequently found in the sclera,

epidermis, and, occasionally, in the nails. It is excreted in the urine which is dark. Cases of the disorder may be divided into those due to the circulation in the blood of certain aromatic compounds with the excretion in the urine of (a) homogentisic acid, (b) melanin, and (c) following the external use of phenol. The cartilages of the ears and nose have a peculiar bluish tint. The blackened appearance as of new shined boots is due to a melanin type of pigment in the cartilage, not the perichondrium. There may be dark pigmented spots in the sclerae and patches of pigmentation in the skin (Seaborn: J 110: 676, 1938 Smith: Ib. 120: 1282, 1942)

## AMYLOIDOSIS

The skin, as well as internal organs, may be the site of deposits of amyloid, a homogeneous degenerative substance which iodine stains a mahogany brown and which characteristically is deposited about the endothelium of capillaries. Cases can be grouped (Michelson and Lynch AD&S 32: 363 1935) as (1) localized amyloidosis cutis; (2) generalized amyloidosis with cutaneous involvement (3) systematized amyloidosis with skin lesions.

**Localized Amyloidosis** may be primary or secondary. The eruption, which may be called lichen amyloidosus, is generally composed of firm, seemingly translucent hemispherical papules, smooth and shiny or slightly scaling, brownish or dark brown, or yellowish or livid in color grouped in patches but tending to remain discrete, intensely pruriginous, and situated most commonly on the extensor surfaces of the extremities especially the legs, the flexor surfaces of joints being almost invariably free. Dostrovsky and Sagher (AD&S 44 891 1941) reviewed 5 cases, utilizing in diagnosis the intradermal injection of 0.1 cc of 1 per cent Congo red solution, which stains the amyloid nodules a persisting red. See also Greenbaum and Bauer (AD&S 55: 31 1947) Treatment is unavailing.



Fig 111 — Lichen amyloidosis, leg. (Dr Da id Lieberthal.)

**Generalized Amyloidosis** presents no characteristic eruption. The parenchymatous organs are chiefly involved the skin little. In generalized cases the diagnosis depends on the presence of an enlarged spleen and liver and the hypoproteinemic syndrome (proteinuria, diminished proteinemia, hypercholesterolemia, anasarca) and particularly on the Congo red test (Nomland AD&S 33 83, 1936). This is performed by injecting intravenously 10 to 15 cc of 1 per cent solution of the dye and withdrawing blood samples after 4 minutes and again after 1 hour the first sample being the measure of 100 per cent. Retention of 90 per cent or more is required for the test to be read as significantly positive (Harmon et al. AMA Arch IM 70 416, 1942.) Sore tongue is a typical and extremely distressing feature.

**Systematized Amyloidosis** designates the group of cases which present (1) little involvement of organs usually affected in generalized amyloidosis, (2) involvement of organs ordinarily spared in the commoner form, (3) papular or nodular skin lesions due to deep-seated amyloid deposit (4) deposits that do not react in the ordinary manner to the usual stains, (5) absence of concurrent disease to account for amyloid change. Glossitis with macroglossia is usually an early and painful accompaniment and changes in skeletal muscles give severe aching symptoms. Amyloid infiltrations of the lingual, esophageal, cardiac and skeletal muscles are major features of the 2 cases of Smith and Woolhouse (JPathBact 47 311, 1938). Primary systematized amyloidosis is a rare constitutional disease in which, without apparent cause there is extensive deposition of amyloid throughout the body with a peculiar affinity for smooth and striated musculature and the skin, according to Brunsting and Macdonald (JIn D 8 145 1947). In their 4 cases, the eruption consisted of

yellowish brown pigmentation of the eyelid, mandibular and submental areas, and small, shiny amber-colored papules on the forehead, eyelids, face, neck, hands, trunk, and oral and lingual mucosa. Pinhead to dime size subepithelial ecchymoses appeared at the sites of the eruption. Macroglossia with impairment of speech and swallowing, muscular pains, dyspnea, weakness, and gastrointestinal dysfunction were the features, and, interestingly, Bence Jones proteinuria was found in 3 of the 4 cases, along with sternal marrow changes suggestive of myeloma. Atkinson (MPhChro 193: 31, 1937) had reported amyloidosis in 40 of 643 collected cases of multiple myeloma, and Bence Jones protein was present in 16 of the 40. The nature of this coincidence is not understood. The course is, as a rule, progressively downward.

**Pathology.**—In general amyloidosis the brunt of the disease is borne by the parenchymatous organs. Chronic suppuration, as in empyema, osteomyelitis, or cavitating tuberculosis, is generally the causative factor. Amyloidosis has been provoked in experimental animals by injection of sodium caseinate by Kuczynski, who noted that amyloid was produced after the reaction to the injection ceased to be febrile; and Jaffé (APath 1: 25, 1926) was able to alter collagenous tissue into amyloid-like tissue by inducing hypersensitivity to abnormal proteins.

The structureless or slightly granular amyloid substance is found in greater or less quantity about the capillaries of the dermis and dermal papillae, lying beneath the epidermis and separated from it by a thin layer of connective tissue, also about the cutaneous appendages in the deeper layers and in masses that may even enclose fat cells. Its presence calls forth no inflammatory or foreign body reaction.



Fig. 537.—Amyloidosis, histologic lesion. (Abramowitz and Ludwig: ADS 40: 12, 1939.)

In a study of the occurrence of amyloid deposits in the skin, Freudenthal (AfDeS 162: 40, 1930) found them present in 16 of 60 specimens of keratoma, in 40 of 600 epitheliomas examined, in lesions scattered over the body and in the normal appearing skin of 8 patients with lichen amyloidosis, in 8 of 10 cylindromas from the face, and in unique cases which respectively resembled mild facial erysipelas, redness and swelling of the face, an epithelioma-like lesion of the face and a curious livid nodule on the cheek. He found in rare instances intra-epitheliomatous inclusions of amyloid, and amyloid clumps between the epithelial cells of the epidermis.

## COLLOID DEGENERATION OF THE SKIN

**Colloid Degeneration (Hyaloma, Colloid Milium)**, a chronic and rather rare affection, is characterized by the occurrence of pinhead to split pea size, rounded, yellowish, pellucid nodules. The lesions develop gradually and occur as a rule on the forehead, nose, and cheeks. The nodules are pale orange-yellow in color and of firm consistency. They exhibit a tendency to grouping but they never coalesce. They superficially resemble vesicles, but when incised only a small amount of gelatinous substance can be squeezed out. They give rise to no subjective symptoms, but are persistent.

**Etiology and Pathology.**—The cause is not known. The majority of the reported cases have occurred in adults. The sexes are about equally affected. Long

continued exposure to the weather may be a factor Neither the sebaceous nor coil glands are directly involved. Changes occur mainly in the connective tissue of the corium, especially in the periglandular regions and consist of colloid degeneration of both the collagen and the elastic fibers.

Predisposing factors include long continued exposure to the elements, occupation, and sunlight. Labadie (ADS 16 150, 19[illegible]) thought colloid degeneration best classified under the simple degenerations.

Jager (ADS 13: 629 1925) studied a case in a man of 49 by the aid of differential stains. He found cystlike areas, sharply demarcated consisting of homogeneous, acidophilic material, masses of which were between hair follicles and separated from the epidermis by a slender band of connective tissue. In most sections colloid was divided into irregular segments, with cells along the lines of division suggestive of remnants of blood or lymph vessels. Other cells with relatively large, oval nuclei, and cytoplasm containing vacuole-like bodies, were also found in a few sections, representing surviving endothelial cells of otherwise destroyed blood and lymph vessels.





Fig. 558. Fig. 559.

Fig. 558.—Gouty tophi. (Dr J W Perkins.)
Fig. 559.—Colloid milium. (Dr J D. Moore.)



Fig. 560.—Colloid degeneration of the skin. (Dr John H. Labadie.)

The elastic fibers were swollen and broken int short segments, but not greatly diminished in number Relatively large masses of collacin (Unna) were found, especially in the smaller and incompletely developed lesions. Degeneration of the connective tissue sheaths of the hair follicles was present Chemically, Jager found the colloid-like material t be insoluble in water acetic acid, and alcohol. Testing for pseudomucin it was boiled in 2 per cent hydrochloric acid and neutralized, but it did not reduce Benedict s solution. Tests for amyloid were negative.

Elastic tissue was absent from the masses of amorphous material in the pseudocysts of the corium, which comprised the flat, shiny papules on the dorsa of the hands of the patient reported by Macleod et al. (BJD 44 [illegible] 41 194[illegible]); but the blood vessels and accessory epidermal structures were unaffected.

**Diagnosis.**—The disease is to be differentiated from milium, xanthoma, hydrocystoma, syringocystadenoma, adenoma sebaceum, and benign cystic epithelioma. Resort must be had to a biopsy.

**Treatment.**—The nodules may be destroyed by curettage, the electric needle or by deep freezing with carbon dioxide snow. X-ray treatment is unavailing. Vitamin C may help (Way and Haag: ADS 44: 1147, 1941). See Reuter and Becker (ADS 46: 695, 194[illegible]); Arnold (ib 48: 762, 1943), hand case with staining reactions resembling keratin; Hand (ib 49: [illegible]34, 1944); Robinson and Tasker (ib 52: 180, 1945), cured by vitamin C. Of 8 cases, 3 healed spontaneously on change of climate, and the favorable influence of vitamin C was noted in some by Gilbert and Cox (MJAustral [illegible] 1, 1946).

## SCLERODERMA AND RELATED INDURATIVE DERMATOSES

**Scleroderma** is a chronic dermatosis characterized by boardlike hardening and immobility of the affected skin. The ivory-colored patches may be circumscribed or diffuse. Swelling, hypertrophy, calcification, perhaps, and eventual atrophy of the collagenous tissues are the features.

**Diffuse Scleroderma.**—The initial manifestations may be those of edema, or the affected areas may present more or less evidence of fibrosis from the first. The majority of cases occur in adult life. The affected skin is pinkish in color, smooth and waxy, and pits slightly on pressure. The patches may develop insidiously or rapidly, and vary greatly in size and contour. At the margins they gradually shade off into the sound skin. The sites of predilection are the limbs, face, and upper half of the body. After the disease has existed for some time the skin becomes hard, yellowish, ivory-like and firmly adherent to the underlying tissues. The face may become masklike and expressionless, and the hands assume a clawlike appearance: sclerodactylia.

Scleroderma affects also subcutaneous and deeper tissues, producing interference with respiration and ankylosis of the joints, so that the patient becomes pitiably helpless (O'Leary and Nomland: AmJMSc 180: 95, 1930). It may cause a characteristic form of pulmonary fibrosis (Murphy et al.: J 116: 499, 1941) with cystic bronchiolar hyperplasia (Getzowa: APath 40: 99, 1945). Esophageal involvement causes dysphagia with blocking of firmer foods, sometimes necessitating gastrostomy (Weissenbach et al.: BSocfrancD 44: 1060, 1937). Atony, diminution of peristalsis, and stenosis are found on fluoroscopy, and frequent dilation with small sounds may be helpful (Olsen et al.: IntM 10: 189, 194[illegible]). Heart failure with peculiar myocardial scarring was reported by Weiss et al. (AIntM 71: 749, 1943).

Calcium and phosph[illegible] are [illegible]etained in the body [illegible] scleroderma, and urinary excretion [illegible] small [illegible] large doses [illegible] [illegible]sterol produce marked increase in urinary calcium excretion and help patients but do not cure them, noted Cornbleet and Struck (ADS 35: 188, 1937). [illegible] Gen [illegible] 4 1947) thought [illegible] the treatment of choice. Ingel (ADS [illegible]0 [illegible] 1944) obtained improvement with Padutin, 10 unit [illegible]. Vasodilat[illegible]on with sodium nitrit[illegible] yielded benefit for Cipollaro (ADS 53: 331, 1946). Bern[illegible]tein and Goldberger (ADS 50: 220, 1944; J 130: 570, 1946) have had success with dihydrotach[illegible]sterol. The patient should reside in a warm, equable climate, and physical therapy with baths and massage ha[illegible] value. Sympathectomy and parathyroidectomy are of questionable value. Neostigmine and whole pituitary gland extracts may be palliat[illegible] [illegible] See Hawley: NOrMSJ 9[illegible]: 6, 1939, clinical; [illegible] 1, biochemical; Ochsner and DeBakey: [illegible], surgical aspects.)

**Acrosclerosis** is a syndrome in which are combined features both of Raynaud's phenomenon and scleroderma. As described by O'Leary and Waisman (ADS 47: 382, 1943) the early symptoms appear to be due to intermittent arteriolar spasm of the upper extremities, and sclerosis appears contemporaneously or at some time, even years, afterward. The lower extremities are involved less, may even escape. Facial sclerosis



Fig. 141.—Scleroderma leading to atrophy.



Fig. 142.—Morphea.



Fig. 143.—Scleroderma: degeneration of collagen and atrophy of epidermis.

develops with the sclerodactylia or later. In fully developed cases, the skin of the fingers and hands is smooth, shiny and tense and pale, cyanotic or mottled in color. The terminal phalanges are tapering or rounded, the integument here being rubbery or hard and bound fast to underlying structures. Proximally there is progressive decrease of induration, which seldom extends above the elbow. The hands and fingers are cool and moist.



Fig. 564.

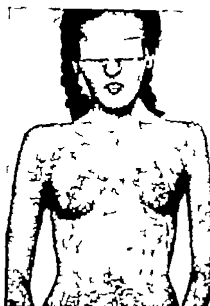


Fig. 565.



Fig. 566.

Fig. 564.—Guttate morphea of 2 years' duration in a girl 14 years old. Lesions appear t follow sympathetic innervation. (Dr Grover Wende.)

Fig. 565.—Generalized ad anced scleroderma. (Dr O. G. Costa.)

Fig. 566.—Deep scleroderma, showing fibrous extensions beset atrophic muscle fibers. (Dr F D. Weidman.)

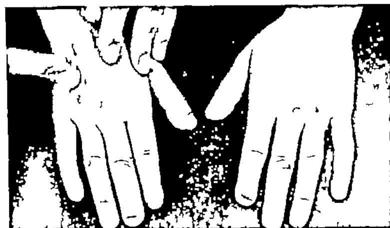
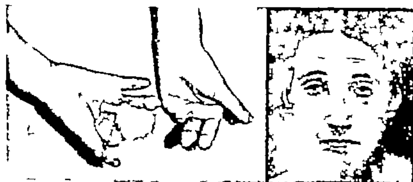


Fig 567 — Acrosclerosis: tense, smooth skin over fingers and hands, clubbing of nails, and shortening of terminal phalanges. (O'Leary and Waisman, ADS 47: 381, 1943.)



Figs. 568-570. — Early acrosclerosis, illustrating diminished mobility of features, puckering of lips and chin, and inflexibility of skin. (Drs O'Leary and Waisman.)



Figs. 571 and 572. — Advanced acrosclerosis with mutilation of hands, necrosis of finger tips, and "ironed out" facies. (Drs. O'Leary and Waisman.)

The fingertips may show scaling fissuring, crusting or ulceration and scars, and calcareous deposits may be present in them Facial skin becomes drawn and stretched with smoothing of the lines of expression. It is not hard but rather taut. Sclerosis fades over the neck and upper chest. Small telangiectatic macules are sometimes present. While the scalp may share the abnormality alopecia does not result After the hands, forearms, face, and upper chest have become involved it is unusual for further extension to occur But the chest may become stiff and the vital capacity reduced, and the patient is considerably handicapped. The abnormalities faded markedly over a period of years in some of O Leary and Waisman s patients, but did not entirely disappear

These authorities regard *sclerodactylia a a potential complication of Raynaud's* syndrome and would combine scleroderma with Raynaud s phenomenon and Raynaud s phenomenon with sclerodactylia in the one title as Hutchinson, whom they quoted did in 1893 The cause is unknown. Prognosis is more favorable than in diffuse scleroderma. If sclerosis has not extended beyond acral parts i * years, generalization is unlikely to take place subsequently The case of Hollander and Vogel (PaMJ 43: 1049, 1940) was unresponsive to therapy Fibrous and cystic lung changes were present in 3 patients of Dostrovsky (ADS 55 1 1947) Jackman (Radiol 40 163, 1943) discussed roentgenographic findings. Interrelationships with dermatomyositis (q v) interested O Leary (CanadMAJ 48 410 1943)

Sclerodactylia like changes occurring in 30 of 178 cases of myocardial infarction seemed due to anoxia and reflex vasoconstriction (Johnson AnnIntM 19 433, 1943)

**Circumscribed Scleroderma (Morphea)** is characterized by the occurrence of one or more circumscribed, grayish plaques, which are usually surrounded by delicate violaceous areolae Occasionally the plaques are elongated and bandlike rarely they may be distributed as if along the course of a cutaneous nerve The course of the lesions is variable The erythematous stage may be prolonged for weeks or months. The plaques may disappear spontaneously leaving little or no trace or they may give rise to circumscribed atrophic areas which persist indefinitely Bulla formation is sometimes seen (Templeton ADS 43 361 1941) The lesion sometimes is a vertical midline stripe on the forehead en coup de sabre Such cases sometimes affect the gums, too (Barber BJD 56 94 1944 Davis and Saunders ADS 54 133 1946) Histamine ointment (Imadyl) and x ray therapy are helpful in the early stages when infiltration exists Stokes (ADS 53 65 1946) favors injections of bismuth see Flood and Stokes (ADS 57 810 1948) Dennie and Morgan (SMJ 40 860 1947) reported success with fever therapy induced by hot baths and the administration of cod liver oil

**White-Spot Disease** is loose designation for any one of several different disorders which manifest small, depigmented atrophic lesions including morphea atrophic lichen planus, and lichen sclerosus (Wise and Sheltmire ADS 17 179 1928 Montgomery and Hill: ib. 42 755 1940) For diagnostic features, see each of these

**Dermatomyositis** is an acute subacute or chronic disease of unknown origin, characterized by a gradual onset with vague and indefinite prodromes, followed by edema, dermatitis and multiple muscle inflammation. The dermatitis may resemble erythema, erysipelas urticaria eczema, or erythema nodosum It generally appears over the affected muscles The face especially the eyelids and the extremities, especially the proximal portions are involved Fever is moderate and remittent or intermittent. Sweating is a common symptom [illegible] enlargement of the spleen. In advanced [illegible] the muscles of respiration and deglutition may be involved [illegible] bronchopneumonia or suffocation. The patient of Ingram and Stewart (BJD 46 [illegible] 1934) developed pigmentation and atrophy of the skin [illegible] as well as symptoms of an asthenia gravis Keller (ArchsYBD 193 [illegible]) reported a [illegible] 10 years old, whose symptoms were weakness, edema, and an eruption resembling disseminated lupus erythematosus He noted that 23 cases had previously been recorded as having occurred in children, and 80 in adults

O'Leary and Waisman (ADS 41 1011 1940) collated 40 Mayo Clinic cases, among which 16 were preceded by acute infection such as tonsillitis influenza. Myositis was roughly symmetric the affected muscles being sometimes normal in consistency sometimes doughy or tough and fibrous. Deep reflexes were diminished or lost. Involvement of pharyngeal, laryngeal, or respiratory striated musculature was of bad omen. Cutaneous changes not always present, included erythema, edema, pigmentation, sclerosis, atrophy and efflorescences resembling lupus erythematosus and poikiloderma atrophicans vasculare. Half of their patients died. Schuermann (Abs YBD 1939 p. 57) reported 10 cases and reviewed 263.

The cause is unknown, but staphylococci and streptococci along with focal infection may be significant. The relation to scleroderma is debatable; Dowling and Griffiths (Lancet 1 1424 1939) pointed to the similarities and noted the appearance of Raynaud's syndrome in some cases of both diseases. Keil (AIntM 66 339 1940) and Banks (NEngJM 225: 433, 1941) were impressed with resemblances to disseminated lupus erythematosus (see J 1L: 1150 1939) Calcinosis and symptoms of Addison's disease may also occur as in the patient of Talbott et al. (AIntM 63 438 1939) Calcinosis universalis was present in 4 of the 5 children studied by Hecht (JPediat 17: 791, 1940) A coincidence possibly a relationship with malignant tumor was remarked by Dostrovsky and Sagher (BJD 39 32, 1946)

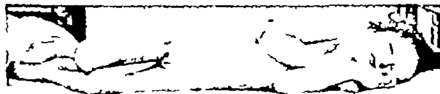


Fig. 572.—Dermatomyositis, a fatal case. (Dr Onis George Hazel.)

Pathologic changes are the corium fat panniculus, and deep fascia. The superficial portion f the dermis is l ttle affected but, deeper one notes edema congestion, hyaline degeneration of fibrous septa, and infiltration of septa and fat lobules with lymphocytic and epithelioid cells, plasma cells and fibroblasts. Inflammatory infiltrate may replace large masses of adipose tissue. The cutaneous histologic changes are not specific (Ki ney and Maher AmJPath 16 561, 1940) nor are those of the muscles; the variability of the manifestations is such that doubt is justified as to whether dermatomyositis is a single li ical entity according to Jaeger and Grossman (AIntM 73 1 1944) Similarities of histologic changes in scleroderma and dermatomyositis were stressed by Freudenthal (BJD 5 289, 1940)

Treatment is emp rical, utilizing rest massage, salicylates and opiates. Prostigmine disappointed Hendry and Anderson (Lancet 1 80 1939) Dihydrotachysterol 20 drops of 0.5 per cent in oil by mouth twice day seemed to explain the recovery of Costello case (ADS 49 459, 1943) Good impro ement followed the use f vitamin C thyroid wheat germ oil, cod li er oil x ray therapy and physical therapy in Cannon's (ADS 51 357 1945) Madden (ADS 53 180, 1946) recommended penicillin intravenously Testosterone may help (Lamb et al. ADS 57 785, 1948)

**Poikilodermatomyositis** is the name pplied t cases with features of dermatomyositis in which atrophy of the ski also occurs. Such ere described by Petges and Cléjat (AnnDerm 7 560, 1906) clarified by G y et al. (ADS 40 56 1939) Areas of skin became inflamed early then atrophic with telangiectases and pigmentation. Sclerosis and calcinosis may also occu in these cases (Hopkins ADS 39 761 1939 Horn ib. 44 1048 1941; Kanee: ib. 50 34 1944) High creatinuria due to destruction of muscle tissue is a common feature noted Traub (ADS 4 734, 1943) whose case resembled disseminated lupus erythematosus

**Scleredema** haract rized by benign but progressive induration and swelling of the skin and subcutaneous tissues The skin is smooth and its consistency much increased but it does not pit on pressure Sensation is unaffected. There is no atrophy pigmentation, or hair loss, and there are signs f inflammation. The changes ften begin at the nape of the neck and spread over the face d trunk, affecting the lower part of the body generally t lesser degree The condition usually follows some febrile disease Pleural effusion pericardial effusion and hydrarthroses are said

occasionally to occur (Vallee NEngJM 235: 207 1946) It eventually disappears spontaneously, little influenced by treatment (Epstein: J 99: 820, 1932) O'Leary et al. (AmJMSc 199 458, 1940) reviewed 15 cases and recommended artificial fever massage, and elimination of focal infection. Piffard described the condition in his text in 1876 (Saffron: ADS 47: 110 1943) although credit is usually given to Beckle (KlinWchs 39: 955 1902)

Cadaveric Induration, unlike subcutaneous fat necrosis is seen in debilitated and premature infants (Ballantyne quoted by Gray: BJD 45: 498, 1933) It may appear suddenly on the third or fourth day or any time during the first weeks of life, without apparent cause except undernourishment and debility or at a later age in babies with gastrointestinal disorders, especially severe diarrhea, resulting in dehydration The lesions are manifest first on the lower extremities, usually on the calves and they extend upward rapidly to involve the entire body The disease is fatal in the great majority of cases, the duration being only a few days as a rule. Many cases ere seen during the siege of Leningrad (Antonov JPed 30 250 1947) Compare lipo granuloma p. 11

## RELAPSING FEBRILE, NODULAR, NONSUPPURATIVE PANNICULITIS

The lesions in this rare disease are irregular or rounded, bluish or erythematous nodules of 0.5 to 10 cm. in diameter They appear at irregular intervals of weeks or months, without relation to season. Fever and malaise accompany their appearance. The lesions occur on the trunk or extremities, but mainly on the thighs. As the lesions undergo involution, subcutaneous atrophy results in the production of depressions. The cause is unknown (Bailey J 109 1419 1937) Diabetes mellitus complicated the 4 cases of Machacek (JInvD 10 ?15, 1948)



Fig. 574.

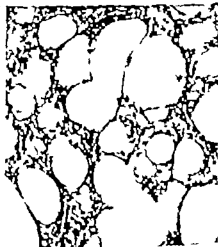


Fig. 575.

Fig. 574.—Panniculitis lesion of legs. (Christi AJ (M 42 ... 1935.)
Fig. 575.—Panniculitis histologic lesion. (Bailey J 109 1419 1937)

The lesion would gradually enlarge making dull red elevations as they reached the surface become fluctuant discharge and heal with scarring in the patient of Ayres (ADS 54 300 1946 Early lesion resembled morphea in the young girl of Harri and Lamb (OklaSMAJ 33 1 1940) Binkley (J 113 113 1939) noted that 11 of the 13 reported cases were females among whom obesity was common. Sterile yellow green, mucoid material was aspirated from lesions, some of which ... ed the breast in his patient and resembled traumatic lipogranuloma. Sulfapyridine relieved the case of Arnold (ADS 51 94 1945) for a prolonged period, but relapse fever and increase of sedimentation rate appeared when the drug was discontinued. Penicillin apparently cured a patient of Zee J (130 1 19 1946) after sulfonamide had failed.

## CALCIFICATION IN THE SKIN (CALCINOSIS)

True osteoma (q v) has been observed in the skin. Calcification occurs locally too in arteriosclerotic patches, caseous tuberculous nodules, laparotomy scars (rarely) chronic inflammatory lesions, fat necrosis secondarily vascular thromboses, scleroderma, dermatomyositis, and some new growths such as atheroma, dermoid cysts, basal cell epithelioma, calcifying epithelioma, fibroma, sarcoma, and pseudoxanthoma elasticum.

**Local Calcium Deposits** in scars generally have followed severe blunt force but sometimes develop in clean wounds (*Lewis: SGO&Am 1 1119 1917 Bouton: Thèse, Paris, 1935*)

Calculi are found occasionally in the umbilicus and beneath the prepuce. Thomas (UCutRev 41: 318, 1936) listed 3 types of preputial calculi: smegma concretions, composed of cells, lipoid matter bacteria, and lime; concretions composed mainly of phosphate from urine retained in the preputial sac and migratory stones, i.e., those formed elsewhere.

**Metastatic Calcification.**—The lungs, stomach, and kidneys are the main sites of deposition of calcium as a result of excessive absorption from the normal depots (Weidman and Shaffer ADS 14 503 1926) This may occur in leukemia, metastatic new growths, hyperparathyroidism and osteomyelitis, and is associated with hypercalcemia (Maloney and Bloom ADS 23: 245 1931; Grayzel and Lederer: AIntM 64 156, 1939) It is a hazard of vitamin D overdosage.

**Metabolic Calcinosis** is manifested by abnormal deposition of calcium salts in the skin, subcutaneous tissues, and superficial fascia in plaques and nodules of 1 to 4 mm. diameter usually affecting the extremities and tendon insertions, occasionally with perforation and discharge through the skin, at times associated with scleroderma, and not associated with excess of calcium in blood or urine (Graham ADS 41 864, 1940)

Calcinosis falls into 2 main classes (1) *calcinosis universalis*, the general, diffuse, or metabolic form, and (2) *calcinosis circumscripta*, a more localized form of which many cases have been described under the title of hypodermolithiasis, or chalk gout (Rosenberg: J 116: 1791 1940)

Calcinosis Universalis.—Tumors or plaques, from pea to walnut size, appear under or in the skin, involving the region of larger joints and even the back. The overlying integument becomes red and adherent; perforation occurs with the discharge of creamy oleaginous, gritty material; the indolent, sluggish ulceration heals with scarring; and the involvement leads to contractures inanition and eventually in many cases, to death. The wrists, knees, elbows, and hips are the most usual sites. The course extends over a period of years. See Brooks (QJM 3: 293 1934) Rothstein and Welt (AmJDisChild 52: 368, 1936)

Calcinosis Circumscripta.—This type involves the upper extremities, especially the hands and elbows. Swelling of the phalanges occurs and calcareous nodules develop. These may rupture and discharge. *There is some interrelationship with nodular xanthoma*, which affects the same locations and in the lipid of which calcium may be deposited, and with Raynaud's disease and sclerodactylia, which are presumed t be associated with dysparathyroidism.

Etiology and Pathology.—Patients have ranged in age from a few month t senility There is no predilection as to sex. Roentgenologic examination reveals typical subcutaneous deposits of opaque substance (urates do not obstruct the rays) Chemical analysis shows the composition f the minerals to be calcium phosphate and carbonate, the phosphat predominating in pproximately the proportions found in normal bone. On pathologic examination, the calcification is seen to involve swollen and retrogressively changed fibrous tissue. The blood calcium and phosphorus levels are generally normal. The basis f bone formation in the skin is always pathologically altered tissue. Robison (BiochemJ 17: 286, 1923) believed that phosphatase enzyme plays an important part; acting on phosphoric acid ester it liberates phosphoric acid, which attaches calcium to itself. According to Klotz (JExpM 7 633, 1905, calcification depends upon the intervening formation of soaps. Harper (APath 3 14, 1927) produced metastatic calcinosis in dogs by means of the administration of parathyroid extract. We interpret calcinosis as being closely related to xanthoma, for if the lesions of xanthoma tuberosum underwent calcification, the picture would be that of calcinosis universalis. Calcinosis is perhaps xanthomatous metabolic mismanagement of lipoid in conjunction with hyperparathyroidism.

Treatment.—Excision of osteomas and of localized calcium deposits is satisfactory. In universal calcinosis, Craig and Lyall (BJChildDis 28: 29 1931) recorded benefit with sodium acid phosphate 3 Gm daily, and Kennedy with a ketogenic diet. Epstein et al. (ADS 21: 510 1933) found ineffectual the usual low calcium, low vitamin diet with the disodium phosphate acidifier; they advised symptomatic treatment with incision and drainage when needed and suggested the trial of hyperpyrexia. We have had striking success in one case, first seen in 1933 with the subcutaneous administra-



Fig. 476.—Calcinosis universalis, lesions of elbow



Fig. 477.—Calcinosis universalis. (Epstein, et al. ADS 21: 267 1933.)



Fig. 478.—Calcification in calcinosis. (Dr. Fred W. Klemm.)

tion of an active parathyroid extract given to tolerance on alternate days. Roentgen examinations proved that this treatment, prolonged in our patient, did not decalcify the skeleton. Sodium acid phosphate has been given to this patient continuously. *Adhesive tape applied to the plaques prevented their ulceration.* She died in 1946 of carcinoma of the ovary.

## HYDROA VACCINIFORME, LIGHT SENSITIVITY DERMATOSES, AND PORPHYRIA

**Hydroa Vacciniforme (Hutchinson's Summer Eruption)** is a recurrent, vesicular dermatosis which occurs in the summertime chiefly in young persons, usually involving only the uncovered skin. This rare affection appears in early life and gradually subsides following puberty. The lesions develop in crops and consist of pinhead- to pea-sized vesicles, or small, acuminate papules which later undergo vesiculation, and are usually confined to the cheeks, nose, ears, and backs of the hands. Symptoms of itching and burning are comparatively slight. The duration of an individual vesicle is from 3 to 7 days, after which the lesion, which often exhibits more or less umbilication, becomes inspissated, and a yellowish or reddish crust forms, soon drops off and leaves a sharply defined pitlike cicatrix. By the development of new lesions an attack may be prolonged for several days, although the average exacerbation seldom extends over a fortnight. Scarring is sometimes extensive. Occasionally two cases occur in one family.

**Hutchinson's Summer Prurigo (Prurigo Aestivale)** is the title applicable to mild cases of hydroa in which recurrent eruptions of prurigo-like papules appear, their earliest manifestation being erythema and urticarialike swelling. On the face there may be similarity to lupus erythematosus. Vesicles may be present but the eruption is variable, phases of sensitivity to sunshine alternating with apparently partial or temporary desensitization. Distinction between hydroa vacciniforme and prurigo aestivale is ambiguous.

Pick (AfDuS 146: 466, 1924) based the differential diagnosis on the following criteria. Hydroa vacciniforme begins in early youth and shows predilection for males; colliquative vesicles are the primary lesions. It leaves scars, is characterized by itching and burning, but is not excoriated; and hematoporphyrin is relatively frequently present. Prurigo aestivale begins at a later age than hydroa vacciniforme and shows predilection for females; itching, urticaria-like papules are the primary lesions, the disease disappears in the winter, intense pruritus prevails, lichenification from excoriation develops even extensively, and no hematoporphyrin is demonstrated. These criteria of Pick, quoted and examined critically by Epstein (JInvD 5: 187, 1942), are not valid, Epstein stated, because (1) about one third of the cases of hydroa vacciniforme begin before the *third year of life and about four fifths before the fourteenth year.* Prurigo aestivale does not start so frequently in childhood, but all 5 original cases of Hutchinson's which Pick recognized as prurigo aestivale started at ages ranging from 8 to 15 years; earlier ages of onset have been reported. (2) Predilection for males in hydroa vacciniforme is generally asserted and this is true of familial cases, which, however, constitute only 10 per cent of all cases, among which there is actually a preponderance of females, for, in the review of Senear and Fink (ADS 7: 145, 1923) of more than 60 cases of hydroa vacciniforme, females led two to one. (3) The primary lesion of hydroa vacciniforme is urticarial, not vesicular. Blisters do not appear in all cases. (4) Mild eruptions of hydroa vacciniforme frequently heal without scars, and scars are not rare in prurigo aestivale. (5) There is no proof that porphyrins play a causative role in either prurigo aestivale or hydroa vacciniforme, but porphyrins have been demonstrated in some cases of both conditions. In summary, typical cases of either condition present a clinical state easily recognized, but there is no single criterion which will allow a hard and fast differentiation.

**Eczema Solare**, a term introduced by Willan, comprises a heterogeneous group of photodermatoses which have in common more or less acute dermatitis following exposure to the sun. Epstein (JInvD 5 187 1942) distinguished among these (1) cases combined with or closely related to urticaria photogenica, (2) cases of eczematoid dermatitis partially or temporarily simulating prurigo aestivale (3) cases of solar dermatitis,



Fig 579



Fig. 580

Fig 579.—Hydroa aestivale (Dr George M MacKee)

Fig 580.—Eczematous dermatitis in a case of pathologic porphyrin formation in the bowel, with hepatopathy (Urbach KlinWchn 17 384, 1938.)



Fig. 581



Fig. 582.

Fig. 581.—Hydroa acneiforme (Dr J. B. Shelmire.)

Fig. 582.—Hydroa vacciniforme, histologic lesion.

vesicular but without urticaria or prurigo and (4) cases which morphologically and etiologically belong to contact dermatitis.

Three types of pathologic reactions to light were distinguished by Epstein (JInvD 5: 225 1942): (1) *immediate urticarial reactions* These never occur in normal persons and they start with erythema, usually accompanied by pruritus, which develops within a few minutes after irradiation begins, may comprise with small exposures merely ½ to 1 hour of erythema only and may with larger doses comprise urticaria limited to the test site, or with adequate exposure, complete wheeling which exceeds the test site by a few millimeters; ( ) *pathologic sunburnlike reactions* these differ mainly quantitatively from normal ultraviolet reactions often occurring in patients of the prurigo aestivale group; and (3) *reactions producti e of lesions characteristic of prurigo.* Such reactions Epstein summarized as follows: (A) Irradiation of previously diseased skin may lead to local provocation of prurigo w thin a few hours, or provocation of prurigo on other previou ly diseased or tested, but not irradiated, parts, or no prurigo eruption on parts previously not diseased; (B) Irradiation of normal skin, previously not diseased, may lead to no eruption on irradiated parts, or prurigo after 5 to 9 days, or prurigo after 2 to 4 days or prurigo at sites previously diseased but not irradiated.

These 3 types of reaction seem to be independent of each other and to correspond essentially to the 3 clinical entities, urticaria photogenica, eczema solare, and prurigo aestivale. Combinations of the types may be postulated to exist in explanation of the variety of clinical manifestations. The three types of light sensitivity are not due to specific wavelengths, for each has been provoked by more than one spectral region.

The provocation of lesions of prurigo aestivale may involve more than specific absorption of certain wavelengths. Local provocation on previously normal skin was, in Epstein experiments, always dependent on the provocation of erythema, without which no prurigo appeared. Intensity of eruption increased in direct proportion to the degree of erythema, which was not necessarily due to ultraviolet, for erythema from other radiation, such as alpha rays, had the same result. That erythema is necessary is indicated further by instances where prurigo was provoked by radiation which normally does not produce erythema. Yellow-red light produced erythema and prurigo in the case of U bach and Konrad (Strahlenther 32 193 1929)

*Phototoxic reaction* and *photoallergic sensitivity* were separated clearly by Epstein (JInD 5: 289 1942) While the mechanisms are different, they are clinically frequently combined. Phototoxicity means primary nonallergic photoreactivity applicable indiscriminately to all individuals and varying quantitatively with the dose. Phototoxicity satisfactorily explains sunburn and the primary sulfanilamide response (Sulzberger Dermatologic Allergy 1940) and plays a role in berloque dermatitis (see contact photosensitization, p. 89) But urticaria photogen ca is not an example of photodynamic action (Blum Photodynamic Action and Diseases Caused by Light Reinhold, 1941) nor can prurigo aestivale be so explained. Epstein theorized that in photoallergic persons a precursor substance or proantigen exists which is altered by light into an antigen. Certain individuals can produce antibodies to such an antigen during a suitable incubation period. Such antibodies may be fixed or circulating. In the sensitized individual proantigen plus light plus antibodies results in dermatitis. Once this has occurred, the reaction time of subsequent reactions is briefer than the incubation time of the first reaction. Some cases prove to have circulating, passively transferable antibodies, and others do not. Antigen produced in the recipient's skin through the action of light must depend upon proantigen transmitted with the donor s serum. While prurigo aestivale may be presented as a photoallergic manifestation, other factors in addition to light sensitivity and allergy may contribute t its pathogenesis.

**Urticaria Photogenica** is manifested by the appearance of wheals at sites which have been exposed to light, such as have been studied by Duke under the designation of physical allergy (see p 31, p 114) While cases of solar urticaria are clinically similar Blum et al. (JInvD 7 99 109 1946) distinguished (a) those due to ultraviolet wave lengths of 3130 to 3650 Å (less than 3700 Å) wherein passive transfer of the patient s serum induces photosensitivity of the same wavelength limits locally in the normal recipient s skin, from (b) those due to blue and violet wave lengths of 4000 to 5000 Å, wherein passive transfer cannot be accomplished, the condition is of sudden onset, and habitually exposed areas are sig

deficiency conditions there is often a complicated interlinking of one substance with another (Spies et al. Am J M Sc 200 536 1940) The full blown deficiency diseases are usually recognized, but the minor symptoms of deficiencies that are common are regularly missed unless kept in mind and searched for Glossitis or an atrophic tongue as well as peripheral nerve disturbances, should always bring to mind vitamin B deficiency Easy bruising and unexplained edema should make one think of a deficiency in vitamin C The deficiency may be due to a deficient intake of the specific food factors for normal needs, an insufficient supply for abnormal needs as in pregnancy a defect in absorption, or a disturbance in utilization. To fulfill its purpose, a nutritional factor not only must reach its point of use in sufficient amount but must actually be used there (Haden J 106 261 1936)

**Vitamin Deficiencies** were epitomized by the Council on Foods and Nutrition of the A.M.A. (J 131 666 1946): Deficiencies of several vitamins, notably biotin, pyridoxine pantothenic acid and vitamin E, are not accompanied by stigmas which can be recognized at present. The subject is in a stage of fluidity and development which probably will necessitate early revision or amplification. Particularly is this true of the diagnosis and treatment of deficiency of folic acid. Not many of the stigmas listed are diagnostic of a vitamin deficiency in themselves, but the occurrence of several of these stigmas in association is at least presumptive evidence of some nutritional failure. Vitamin deficiencies commonly encountered in clinical practice are multiple. Scrutiny of the dietary history is indicated in cases in which several of the stigmas listed are present Treatment for a deficiency involves administration orally or if need be parenterally of large enough doses of the vitamin to be of therapeutic value and continuation of this treatment for long enough periods to assure a satisfactory therapeutic trial. However since the diagnosis is necessarily presumptive in many instances, exclusive dependence on specific therapy is justified only infrequently and basic to good treatment in all cases is a diet planned to be adequate nutritionally and assurance that the diet is eaten. Likewise helpful in treatment because of its content of factors not as yet identified is some good source of the vitamin B complex as a whole. Products such as brewer's yeast or an extract of such yeast, wheat germ, extracts of cereal grasses or of rice bran, crude extract of liver or desiccated liver represent such sources. For a patient who cannot take foods or drugs orally or in whom absorption is poor crude liver extract may be given intramuscularly or even intravenously when it may be diluted with sterile isotonic solution of sodium chloride or dextrose and administered by vein.

### STIGMAS SUGGESTING DEFICIENCY OF VITAMIN A

*Xerosis of the conjunctiva*

Thickening with loss of transparency so that only the more superficial vessels of the bulbar conjunctiva are clearly seen, associated with more or less yellow pigmentation, especially along the horizontal meridian of the eyeball; infrequently associated with small foamlike plaques called Bitot' spots.

*Toad skin eruption (pilosebaceous follicle*

A grater-like feel, which in early stages resembles gooseflesh but, when more fully developed, presents the picture of keratosis pilaris. The extensor surfaces of the arms and thighs and the flexor surfaces of the legs are primarily affected.

*Xerosis or asteatosis of the skin*

Dryness, scaliness and crinkling, in extreme cases resembling alligator skin. In early stages the condition is associated with keratosis pilaris but if persistent and extends after follicles have disappeared, the body hairs being broken and partly lost. All parts of the body are involved, but the skin of the extremities particularly of the legs, is more severely affected than the skin of the head and the trunk.

*Follicular conjunctivitis*

Hypertrophy of the follicles, particularly of the lower eyelids.

*Night blindness*

Conspicuous only in cases of advanced, severe deficiency

*Keratomalacia*

Thickening with subsequent ulceration and necrosis of the cornea present only in most severe and advanced forms of deficiency

### TREATMENT OF VITAMIN A DEFICIENCY

*Early deficiency stat*

25,000 U S P units of vitamin A twice daily for two months or longer

*More chronic states*

25,000 U S P units of vitamin A two to three times daily for prolonged period

vesicular but without urticaria or prurigo and (4) cases which morphologically and etiologically belong to contact dermatitis.

Three types of pathologic reactions to light were distinguished by Epstein (JInvD 5: 289 1942): (1) *immediate urticarial reactions* These never occur in normal persons and they start with erythema, usually accompanied by pruritus, which develops within a few minutes after irradiation begins, may comprise with small exposures merely ½ to 1 hour of erythema only and may with larger doses comprise urticaria limited to the test site or with adequate exposure, complete whealing which exceeds the test site by a few millimeters; (2) *pathologic sunburnlike reactions* these differ mainly quantitatively from normal ultraviolet reactions often occurring in patients of the prurigo aestivale group; and (3) *reactions productive of lesions characteristic of prurigo.* Such reactions Epstein summarized as follows: (A) Irradiation of previously diseased skin may lead to local provocation of prurigo within a few hours, or provocation of prurigo on other previously diseased or tested but not irradiated, parts, or no prurigo eruption on parts previously not diseased; (B) Irradiation of normal skin, previously not diseased, may lead to no eruption on irradiated parts, or prurigo after 6 to 9 days, or prurigo after 2 to 4 days, or prurigo at sites previously diseased but not irradiated.

These 3 types of reaction seem to be independent of each other and to correspond essentially to the 3 clinical entities, urticaria photogenica, eczema solare, and prurigo aestivale Combinations of the types may be postulated to exist in explanation of the variety of clinical manifestations. The three types of light sensitivity are not due to specific wavelengths for each has been provoked by more than one spectral region.

The provocation of lesions of prurigo aestivale may involve more than specific absorption of certain wavelengths. Local provocation on previously normal skin was, in Epstein's experiments, always dependent on the provocation of erythema, without which no prurigo appeared. Intensity of eruption increased in direct proportion to the degree of erythema, which was not necessarily due to ultraviolet, for erythema from other radiation, such as alpha rays, had the same result. That erythema is necessary is indicated further by instances where prurigo was provoked by radiation which normally does not produce erythema. Yellow-red light produced erythema and prurigo in the case of Urbach and Konrad (Strahlentherapie 32: 193, 1929)

*Phototoxic reaction* and *photoallergic sensitivity* were separated clearly by Epstein (JInvD 5: 289 1942) While the mechanisms are different, they are clinically frequently combined. Phototoxicity means primary nonallergic photoreactivity applicable indiscriminately to all individuals and varying quantitatively with the dose. Phototoxicity satisfactorily explains sunburn and the primary sulfanilamide response (Sulzberger Dermatologic Allergy 1940) and plays a role in berloque dermatitis (see contact photosensitization, p. 80) But urticaria photogenica is not an example of photodynamic action (Blum: Photodynamic Action and Diseases Caused by Light, Reinhold, 1941) nor can prurigo aestivale be so explained. Epstein theorized that in photoallergic persons a precursor substance or proantigen exists which is altered by light into an antigen. Certain individuals can produce antibodies to such an antigen during a suitable incubation period. Such antibodies may be fixed or circulating. In the sensitized individual proantigen plus light plus antibodies results in dermatitis. Once this has occurred, the reaction time of subsequent reactions is briefer than the incubation time of the first reaction. Some cases prove to have circulating, passively transferable antibodies, and others do not. Antigen produced in the recipient's skin through the action of light must depend upon proantigen transmitted with the donor's serum. While prurigo aestivale may be presented as a photoallergic manifestation, other factors in addition to light sensitivity and allergy may contribute to its pathogenesis.

**Urticaria Photogenica** is manifested by the appearance of wheals at sites which have been exposed to light such as have been studied by Duke under the designation of "physical allergy" (see p. 31 p. 114) While cases of solar urticaria are clinically similar Blum et al. (JInvD 7: 99 109 1946) distinguished (a) those due to ultraviolet wave lengths of 3130 to 3650 A (less than 3700 A) wherein passive transfer of the patient's serum induces photosensitivity of the same wavelength limits locally in the normal recipient's skin from (b) those due to blue and violet wavelengths of 4000 to 5000 A wherein passive transfer cannot be accomplished, the condition is of sudden onset and habitually exposed areas are dis

nificantly less sensitive to light than the areas usually covered by clothing. In type (a) the patient is not only extremely sensitive to the wavelengths that produce sunburn in normal persons, but the sensitivity extends to longer wavelengths so that the patient whose urticarial response is elicited by a much larger fraction of sunlight may suffer even in winter from *relatively short exposures and is susceptible to radiation through window* glass, which almost completely protects normal persons.

**Porphyria,** according to Brunsting and Mason (PSMDIC 22 489 1947) whose article prior to publication is our source here extensively quoted is that rare familial metabolic fault in which abnormal kinds and amounts of porphyrins, especially uroporphyrin, are excreted in the urine and feces. The disease may be asymptomatic for years or for life and the urine may or may not have an abnormal coloration. Surveys of families in which this inborn error of metabolism occurs may disclose the presence of uroporphyrin or colorless porphobilinogen in the urine of apparently normal persons. Little is known of the factors which may precipitate *the manifest syndrome of* porphyria or influence its course. *In certain* cases, a damaging influence on the liver either by disease such as cirrhosis or by hepatotoxic drugs or poisons (alcohol, barbiturates, arsenic, lead) appears to contribute to the development of obvious symptoms.

Porphyria finds clinical expression in various forms *the acute type* with intermittent episodes of serious gastrointestinal or nervous and mental symptoms *the congenital type* which may begin in earliest childhood with red urine erythrodontia, a mutilating eruption of the light exposed skin, and sometimes visceral complications and *the intermediate or chronic types* which may belong to one or the other of the preceding, appearing usually in adults and with a clinical course that is mild as a rule.

Porphyrins possess the power to sensitize the skin to light but the photodynamic mechanism of this process is obscure Attempts to reproduce an eruption in the skin of porphyric individuals by exposing them to sun or to artificial light have been for the most part unsuccessful.

In acute porphyria, pigmentation occurs but other cutaneous reactions are infrequent In congenital porphyria the outstanding change is the reaction to the light-exposed surfaces of the skin Bullous eruptions occur in chronic porphyria as a result of exposure of the skin to light and to minor trauma with the production of lesions similar to those seen in epidermolysis bullosa The latter condition represents a fault in the binding mechanism of the skin with a varied hereditary pattern, but no actual relationship between true epidermolysis bullosa and porphyria has been established

Cases of porphyria were reported by Brunsting and Mason in which the cutaneous manifestation were the presenting symptoms. In each instance a history of chronic alcoholism and evidence of hepatic dysfunction were present, and it seemed reasonable *to relate these facts to the precipitation of the clinical syndrome* Two of the patients, examples of chronic porphyria, had a mild bullous reaction of the exposed skin and uroporphyrin in the urine The other had in addition to the aforementioned symptoms a severe episode of abdominal colic accompanied by uroporphyria and porphobilinogen in the urine example of acute porphyria. In this case they discovered that the mother of the patient had latent porphyria.

The changes which occur in the skin in chronic porphyria are melanosis, hypertrichosis, *milia* and a chemical and physical alteration of the connective tissue which renders the surface layers susceptible to trauma and gives rise to a blistering reaction to light. Only the exposed skin is so affected presumably through the toxic influence of cumulative doses of light, although the blisters cannot well be reproduced by

artificial means and cannot be reproduced at all on the skin that has been protected from light. These changes occur also in epidermolysis bullosa, which is likewise an inherited abnormality of the skin but the two conditions are entirely distinct. In epidermolysis bullosa, trauma alone is the precipitating agent, and the pressure surfaces such as the palms and soles are primarily involved. It would be better to describe the cutaneous manifestations of porphyria as bullosis actinica et mechanica. In porphyria, even on the light-exposed surfaces, blistering is a late manifestation, and the Nikolsky phenomenon can be elicited irregularly if at all. To some extent, the degree of cutaneous reaction in porphyria may be proportional to the concentration of porphyrins in the tissues and to the kind of porphyrin that is concerned as well as to the nature and concentration of the light source and the effect of its cumulative action. Photosensitivity is prominent in those cases in which prophyrins are injected experimentally into the skin and in cases of congenital porphyria, but it is rarely a feature of either chronic or acute porphyria.

The liver frequently is involved in acute porphyria. The changes in the skin in chronic porphyria may be influenced by the abnormal porphyrins which are produced when the liver is damaged by such a toxin as alcohol; or perhaps such a damaged liver may inhibit or destroy protective enzymes essential in the skin for the prevention of reactions to photosensitivity. The chief protection of the skin against light is probably the keratin layer but the value of pigment cannot be dismissed summarily. The production of pigment in the human skin in cases of chronic porphyria is probably a late effect, representing an effort to protect the underlying tissues from penetrating radiation. Milia occur in chronic porphyria in the areas of skin that have been affected by light. They represent invaginated sebaceous secretions which may occur in normal skin about the eyelids and genitalia, or they may occur in the scarred skin in pemphigus, epidermolysis bullosa, or old burns. In recent years, physicians have become increasingly aware of the importance of the subject of porphyria. If careful search were made of members of families in which isolated cases of manifest porphyria occur it is reasonable to suppose that a reservoir of cases of latent porphyria would be uncovered.

The studies on porphyria by Turner and Obermayer (ADS 37: 549 1938) are valuable. *Linser* (AfDuS 79: 251 1906) first recognized the frequent association of porphyria and hydroa estivale. Hematoporphyrin, possessed of notable photosensitizing power was once thought to be the porphyrin excreted in this disease. Later it was learned that hematoporphyrin is never found either physiologically or pathologically.

Porphyrins are constituents of hemoglobin and chlorophyll, and so are widely distributed in animal and plant life. Animal porphyrins are red compounds which fluoresce red in ultraviolet light. Their spectral absorption bands are individually characteristic but stereo-isomers can be distinguished only by complex determinations of melting points of their methyl esters.

The naturally occurring porphyrins of importance are protoporphyrin, coproporphyrin, and uroporphyrin. Porphins, the basic nuclei from which porphyrins are chemically derived, are composed of 4 pyrrole rings united by 4(=CH—) groups, and each pyrrole ring has 2 replaceable hydrogen atoms. Four methyl and 4 ethyl groups replacing these constitute aetioporphyrin and form 4 series of compounds, of which only Types I and III occur naturally (Rimington: ProcRoySocM 32: 1268, 1939 Edit.; BMJ 1: 1004 1939). Hemoglobin comprises globin, a protein combined with hematin, the iron-containing pigment. Hematin is a porphyrin with an atom of iron bound to a nitrogen atom of each pyrrole ring by primary and secondary valences. The porphyrins differ in the positions of substituent groups in the porphin basic nucleus.

Protoporphyrins are derivatives of aetioporphyrin with 4 methyl, 2 vinyl, and 2 propionic acid groups. Coproporphyrins are derivatives with 4 methyl and 4 propionic acid groups. Uroporphyrins are derivatives with 4 methyl and 4 methyl malonic acid groups. Types I and III cannot derive from one another.

Of some 200 cases of hydroa Turner and Obermayer (1938) stated that some 80 gave definite evidence of porphyria. Knowledge of porphyria, they noted, has been built largely around studies of one Mathias Petry whose "prof-kaunchen" life of 33 years, biochemically busy ones, is biographed in a veritable medical library which includes a 260 page volume on his autopsy. The manifestations of hydroa in the presence of porphyria differ considerably, they believed, from those of hydroa without porphyria. Bullae are usually larger and do not show umbilication, and recurrent attacks are accompanied with nervous... Mutilations may become as extensive as in lupus vulgaris. In the presence of porphyria the disease persists as a rule throughout life, while hydroa without porphyria may disappear spontaneously after puberty.

Hydroa is not the only dermatosis associated with porphyria. A number of cases of epidermolysis bullosa have been so associated, and occasional cases of scleroderma,

calcinosis, keloid formation, xeroderma pigmentosum, lupus erythematosus and even hirsuties have manifested the association. Ocular complications have been noted (Stokes AOphth 23: 1131, 1940)

Hepatomegaly and disturbed liver function are not uncommon. Splenomegaly has occurred several times. Blood changes regularly include anemia as a significant feature presumably because erythrocytes are robbed of pyrroles needed for hemoglobin production.

Coproporphyrin and urophyrin have repeatedly been demonstrated in the serum as well as in the urine. The urine, generally described as red, ranges from pale pink to almost black, or it may be normally yellow when passed but becomes dark after exposure to light through oxidation of porphyrinogen and urofuscinogen. Urinary porphyrins are almost always uroporphyrin and coproporphyrin I. Feces are not characteristic but tend to be dark reddish brown, turning darker on oxidation. While coporporphyrin and protoporphyrin are found in normal feces, coproporphyrin in porphyria may be enormously increased.

The teeth show deposition of porphyrin in the dentine and though they may not appear red, brown, or even yellow in ordinary light, ultraviolet illumination discloses red fluorescence

Uroporphyrin and coproporphyrin are less active photosensitizers than hematoporphyrin. But whether their presence explains light sensitivity in hydroa is unproved. Lesions of hydroa are not identical with those of experimental porphyrin light sensitization (Edinow BJD 47 777 1935) nor is there any uniformity of wave lengths of light to which hydroa cases are susceptible, nor do efforts to provoke lesions with light always succeed, nor are all cases of hydroa associated with porphyria, but rather only the minority of them.

**Etiology**.—The cause of hydroa is unknown Exposure to the sun and trauma are strong contributory factors to the existence of dermatitis.

Mathews (APath. 23 399 1937) in a classic review of photodynamic sensitization, found that, in 82 reports which specified, porphyrinuria was present in 23 about a 9 He stated that Raabe in 1900 showed that acridine in a culture of infusoria so altered them that light killed them. The effect is dependent upon the time of contact of the dye with the organism. The action of ordinary light on sensitized protoplasm is similar to the action of ultraviolet of less than 3 100 Å. Eosin, erythrosin, fluorescein, bengal rose and the phylloroporphyrin of buckwheat, as well as hematoporphyrin, have *the capacity of sensitizing it more One can kill frogs by injecting them with eosin* and exposing them to light. Hematoporphyrin is active when given by mouth, subcutaneously intramuscularly or by vein, but painting it on the skin does not photo-sensitize Meyer Betz gave himself 0.2 gm. hematoporphyrin intravenously and was light sensitive for several weeks. Jodlbauer and Busch (1905) produced pruritus, edema, and even necrosis of the skin of the face and ears of experimental animals by so sensitizing them and exposing them to sunlight By injection of eosin and exposure to sunlight, Quin (1933) produced symptoms of bighead in sheep also, by tying the bile duct, he found the icteric skin to have been sensitized by bile secreted phylloerythrin absorbed through the intestine from the chlorophyll rich diet Such observations led Urbach and Block (1931) to believe that the presence of porphyrin signifies hepatic insufficiency

Animal photosensitization can result from diet as in fagopyrism from buckwheat, hypericism (the Arabs painted their horses with tobacco or henna to protect them from the sun when they grazed *Hypericum crispum*) trifoliosis from clover tribulosis from Sudan grass in South African sheep and goat and bighead in sheep and goat fever in southwestern *United States; but no proof exists*, Mathews said, that this occurs in man. Accidental sensitization of man has occurred with intravenous administration of acriflavine In pellagra, light sensitivity is an effect, not a cause of the condition Mathews believed. In eczema solare the appearance and disappearance of porphyrin depend on the appearance and disappearance of the dermatitis (Templeton and Lunsford ADS 37 540 1938)

Proof of the photosensitizational origin of the lesions of hydroa is lacking according to Blum and Pace (BJD 49 465 1937) and the assumption is untenable that all cases of abnormal sensitivity to light have the same cause. Their patient failed to develop lesions when exposed to those wavelengths to which porphyrins sensitize the skin. The normal response to actinic irradiation is not porphyrinuria but in light sensitive patients irradiation may lead to marked increase in porphyria.

Tests for Porphyrins, at least qualitative ones, are fairly simple (Brunsting and Mason 1947). The urine is acidified with HCl and examined visually for fluorescence in a fluorophotometer, the beam being passed through a Corning filter 5113 giving maximum intensity at 4100 Å. If red fluorescence is visible, another sample of urine is acidified with acetic acid and extracted with ether to remove coproporphyrin. Residual red fluorescence which ether extraction does not remove from the aqueous layer indicates the presence of uroporphyrin. Coproporphyrin is present in small amounts in normal urine and in excess in toxic diseases especially those involving the liver. But the presence of uroporphyrin indicates porphyria. The type of porphyrin excreted does not, however, exactly define the class of porphyria present. In acute porphyria, and in affected siblings, colorless porphobilinogen occurs in the urine and is thought a pathognomonic feature of the disease. Porphobilinogen is demonstrated by a modification of the Ehrlich-benzaldehyde test for urobilinogen, the urine being first extracted with chloroform. At times the urine of patients with porphyria may be entirely normal. Quantitative porphyrin determinations were given by Kaligman (ADS 54 281, 1946).

**Other Dermatoses Associated With Light Sensitivity**.—See contact photosensitization (p 89) and xeroderma pigmentosum (p 642). Photodynamic effects were reviewed by Stokes and Beerman (AmJMSc 204 601 1942). See lymphogranuloma venereum.

**Treatment** of all these conditions involves protection from sunlight and trauma. Some photodermatoses may have been successfully hyposensitized by increasing doses of ultraviolet light, Epstein (1942) noted, and ovarian follicular hormone or estrogen has helped some cases (Lain et al SMJ 41 1041 1948). Hydrochloric acid, laxatives, antihistaminics, and niacin may be tried. Alcoholism and hepatic dysfunction should be combated. Brunsting and Mason (J 132 509 1942) recommended procedures for protection of the liver as described by Snell (CalifM 63 74, 1945). A pregnant patient with itchy lesions from porphyria reported by Linns (J 133 105 1947) improved post partum. Solar urticaria, 2 cases of the type caused by wavelengths less than 3700 Å, were relieved by Pyribenzamine so that ultraviolet exposure did not elicit wheals (Rubin et al. JInvD 8 189 1947).

## AVITAMINOSES

Disease may result from the dietary lack of things. The skin exhibits changes due to nutritional inadequacy which may result from insufficient supply at the site of absorption or from inability to utilize the substances or to convert them into assimilable forms, or from excessive requirement because of infection pregnancy or metabolic peculiarity such that the individual demand exceeds that amount which usually suffices to prevent symptoms of deficiency. Solitary dietary faults are the exception for in

| FACTOR | NEEDED FOR INTEGRITY OF |
|---|---|
| Vitamin A | epithelial tissues |
| Vitamin $B_1$ | nerve tissues |
| Vitamin $B_2$ (G) | dermal tissues |
| Vitamin C | endothelium of blood vessels |

| SYSTEM | LESIONS OF DEFICIENCY |
|---|---|
| Epithelium | Atrophy, scaling, dermatitis, pigmentation, ulceration, cornification |
| Nervous system | Neuritis, paresthesias, weakness, paralysis; Degeneration of spinal cord; Tetany |
| Alimentary tract | Anorexia, stomatitis, glossitis, atrophy of tongue, achlorhydria, loss of specific ferment, diarrhea, loss of tone of gastrointestinal tract, ulceration of intestine |
| Hematopoietic system | Macrocytic anemia, hypochromic anemia, microcytic anemia |
| Vascular system | Hemorrhage, easy bruising, edema |

deficiency conditions there is often a complicated interlinking of one substance with another (Spies et al Am J M Sc 200 536 1940) The full blown deficiency diseases are usually recognized, but the minor symptoms of deficiencies that are common are regularly missed unless kept in mind and searched for Glossitis or an atrophic tongue as well as peripheral nerve disturbances, should always bring to mind vitamin B deficiency Easy bruising and unexplained edema should make one think of a deficiency in vitamin C The deficiency may be due to a deficient intake of the specific food factors for normal needs, an insufficient supply for abnormal needs as in pregnancy a defect in absorption or a disturbance in utilization. To fulfill its purpose, a nutritional factor not only must reach its point of use in sufficient amount but must actually be used there (Haden J 106 261 1936)

**Vitamin Deficiencies** were epitomized by the Council on Food and Nutrition of the A.M.A. (J 131: 666, 1946): Deficiencies of several vitamins, notably biotin, pyridoxine pantothenic acid and vitamin E, are not accompanied by stigmas which can be recognized at present The subject is in a stage of fluidity and development which probably will necessitate early revision or amplification. Particularly is this true of the diagnosis and treatment of deficiency of folic acid. Not many of the stigmas listed are diagnostic of a vitamin deficiency in themselves, but the occurrence of several of these stigmas in association is at least presumptive evidence of some nutritional failure Vitamin deficiencies commonly encountered in clinical practice are multiple. Scrutiny of the dietary history is indicated in cases in which several of the stigmas listed are present. Treatment for a deficiency involves administration orally or if need be parenterally of large enough doses of the vitamin to be of therapeutic value and continuation of this treatment for long enough periods to assure a satisfactory therapeutic trial. However since the diagnosis is necessarily presumptive in many instances, exclusive dependence on specific therapy is justified only infrequently and basic to good treatment in all cases is a diet planned to be adequate nutritionally and assurance that the diet is eaten. Likewise helpful in treatment because of its content of factors not as yet identified is some good source of the vitamin B complex as a whole. Products such as brewer's yeast or an extract of such yeast wheat germ, extracts of cereal grains or of rice bran, crude extract of liver or desiccated liver represent such sources. For a patient who cannot take food or drugs orally or in whom absorption is poor crude liver extract may be given intramuscularly or even on occasion it may be diluted with sterile isotonic solution of sodium chloride or dextrose and administered by vein.

## STIGMAS SUGGESTING DEFICIENCY OF VITAMIN A

*Xerosis of the conjunctiva*
Thickening with loss of transparency so that only the more superficial vessels of the bulbar conjunctiva are easily seen, associated with more or less yellow pigmentation, especially along the horizontal meridian of the eyeball infrequently associated with small foamlike plaques called Bitot spots.

*Papular eruptions of pilosebaceous follicles*
A grater-like feel, which in early stages resembles gooseflesh but, when more fully developed, presents the picture of keratosis pilaris. The extensor surfaces of the arms and thighs and the flexor surfaces of the legs are primarily affected.

*Xerosis or asteatosis of the skin*
Dryness, scaliness and crinkling, in extreme cases resembling alligator skin. In early stages the condition is associated with keratosis pilaris but it persists and later extends after follicles have disappeared, the body hairs being broken and later lost. All parts of the body are involved, but the skin of the extremities particularly of the legs, is more severely affected than the skin of the head and the trunk.

*Follicular conjunctivitis*
Hypertrophy of the follicles particularly of the lower eyelids.

*Night blindness*
Conspicuous only in cases of advanced, severe deficiency

*Keratomalacia*
Thickening with subsequent ulceration and necrosis of the cornea present only in most severe and advanced forms of deficiency

## TREATMENT OF VITAMIN A DEFICIENCY

*Early deficiency states*
25,000 U. S. P. units of vitamin A twice daily for two months or longer

*More chronic states*
25,000 U. S. P. units of vitamin A two to three times daily for a prolonged period.

STIGMAS SUGGESTING DEFICIENCY OF RIBOFLAVIN

*Congestion of the limbic plexus*
Visible with a small hand lens or the +20 lens of the ophthalmoscope. Invasion of the cornea by capillaries arising from this plexus (vascularization) requires a biomicroscope and slit lamp for detection.

*Cheilosis*
Represented in chronic deficiency by excessive and irregular wrinkling, in acute deficiency by swelling and erasure of the normal wrinkling of the lips. Reddening, thinning, scaling, chapping of epithelium are associated.

*Angular stomatitis*
Various combinations of erythema and open fissuring in the angles of the mouth with or without a white, moist maceration (perlèche); scars of healed fissures.

*Dyssebacea*
An erythema overlaid with somewhat greasy flaky accumulations resembling hoar frost, noted mostly in the alae nasi, canthi, pinnae and other folds of the skin, accompanied in some cases by coarsening and elevation of the sebaceous follicles of the nose and cheeks, the latter also seen with deficiency of Vitamin A.

*Magenta tongue*
A purplish red coloring with moderate edema and flattening of filiform papilla observed in more advanced deficiency

TREATMENT OF RIBOFLAVIN ($B_2$) DEFICIENCY

*Acute deficiency stat*
5 mg. riboflavin three times daily for weeks.

*Chronic deficiency state*
3 to 5 mg. of riboflavin three times daily for a prolonged period.

STIGMAS SUGGESTING DEFICIENCY OF NIACIN

*Edema of the tongue*
Shown by dental indentations.

*Increased redness of the tongue*
Beefy red in chronic states. Scarlet red in severe acute deficiency

*Congestion and hypertrophy of the papillae of the tongue, followed by fusion and atrophy*
In early stages the fungiform papillae are congested and hypertrophied. This is followed by hypertrophy of the filiform papilla and later by their flattening. As they atrophy they fuse or mat together with multiple fissuring to give a cobblestone appearance and finally baldness. Vincent's infection of tongue and fauces, ulceration and pseudomembrane formation may or may not accompany these changes in the more advanced stages of this deficiency

*Dermatitis*
Erythema, rough scaling, with ulceration and formation of bullae, affecting primarily areas of the skin exposed to light, namely wrists, ankles, neck and face. Observed only in severe deficiency (pellagra) and then frequently associated with diarrhea and dementia

*Encephalopathy*
Clouding of consciousness, cogwheel rigidity and grasping, sucking reflexes observed in acute, severe deficiency

TREATMENT OF NIACIN DEFICIENCY

*Acute deficiency state*
100 mg. or more of niacinamide twice daily for weeks.

*Chronic stat*
100 mg. of niacinamide twice daily over a prolonged period.

STIGMAS SUGGESTING DEFICIENCY OF ASCORBIC ACID

*Redness, edema, tenderness and bleeding on pressure of the gums*
Observed in acute or subacute deficiency of moderate severity, sometimes with, but usually without, other signs of ascorbic acid deficiency

*Thickening and increased firmness of the gums*
With recession and exposure of the base of the teeth, including recession of interdental papillae; observed in chronic deficiency

*Retraction of the gums*
Leaving pockets between gum and tooth, secondary infection and resulting pyorrhea; observed in chronic deficiency

*Loosening and shedding of the teeth.*

*Increased capillary fragility*
Manifested by petechial hemorrhages of the skin, especially in the tourniquet test; observed in more severe acute and subacute deficiency. Easy bruising, spontaneous ecchymoses of the skin, idiopathic hemorrhage into joints and slow healing of wounds, observed in severe acute and subacute deficiency

TREATMENT OF ASCORBIC ACID DEFICIENCY

*Acute or subacute deficiency stat*
100 mg. or more of ascorbic acid for weeks.

*Chronic deficiency state*
100 mg. of ascorbic acid three times daily over a prolonged period.

STIGMAS SUGGESTING DEFICIENCY OF VITAMIN K

*A tendency to bleeding*

Particularly from minor wounds, related to abnormal lengthening of the prothrombin time, developing spontaneously in newborn inf nts observed in adults after treatment with dicumarol or large doses of salicylates in advanced disease of the l er with poor excretion of bile, nd l diseases f the intestine, such as sprue, in which vitamin bsorption is disturbed.

TREATMENT OF VITAMIN K DEFICIENCY

*In dults*

1 mg. f itami K tw to three times daily with or without bile (1 Gm. of desiccated bil or bile salts)

*In newborn babies*

1 mg of synthetic itamin K intramuscularly daily in oil solution for several days.

DEFICIENCY SYMPTOMS

A diagnosis of itamin deficiency only rarely can be based on symptoms or less significant bnormalities than those which have been listed. However such symptoms and abnormalities frequently ccompany the more specific lesions of deficiency

Symptoms commonly observed with deficiency f thiamine, also less conspicuously in deficiency f the vitamins, include pathy lethargy increased emotional irritability hypersensitivity to noise nd painful stimuli, h dache, aguo fears, confusion of thought, uncertainty of memory asthenia, loss of manual dexterity insomnia, heart consciousness, paresthesia, norexia, nausea, flatulence, epigastric pain, constipation. Photophobia, burning of the eyes, lacrimation and eyestrain not relieved by glasses are encountered in deficiency of riboflavin. Other bnormalities unrelated to deficiency of any single vitamin but commonly observed in persons who are malnourished are dry brittle, lack-luster, rebellious, so-called staring head hai a loss of sleekness analogous to the rough coat of malnourished animals, blepharitis, spider lik tela giectasia of the face, seborrhea of the face, patchy pigmentation of the f ce especially suborbital and circumoral, sinus rrhythm , bradycardia, tachycardia, low blood pressure, loss of tone of muscles and anemia.

**Antivitamin Activity** of certain chemical compoun ls closely related to the various vitamins is a well establi hed fact (Edit : J 134 1550 1947) Woolley (PhysRev 27 308, 1947) stated that there is at least one known antivitamin for each of the water soluble tamins and for of the 4 fat-sol ble ones Pyrithiamine when given to mice r rats is followed by la sic symptoms of thiamine deficiency and the effect i nullified if sufficient thiamine is a lministered. I lole acetic acid ha an antiniacin influence (Kodicek et al. Lancet 491, 1947); it was isolated from corn and may be related to the relat e prevalence f pellagra in corn-eating populations. The structure of the ant vitamin is such that it competes w th the metabolite; substituting a sulfonic acid o a ketone for a carboxyl group might make the change but a one way of *changing the molecule is essential. The practical significance of these substances is still* conjectural.

**Vitamin A Deficiency (Phrynoderma)**—The dry shrivelled and scaly skins of infants with nutritional ophthalmia were observed by Block (JHyg 19 283 1921) who showed that some fats contain specific indispensable bodies, the absence of which leads to xerosis, night blindness, and keratomalacia In guinea pigs fed an A-deficient diet Wolbach and Howe (APath 5 239 1928) observed that the epithelium of the lacrimal glands, bladder uterus, and elsewhere underwent squamous metaplasia. The patients of Frazier and Hu (ADS 33 825 1936) presented ocular evidence of avitaminosis A and an eruption resembling keratosis pilaris. Spinous papules appeared at the sites of hair follicles. The microscope revealed hyperkeratinization of epidermis and follicles and squamous metaplasia of sweat duct epithelium There were atrophy of the hair bulbs and cystic degeneration of some of them These symptoms were relieved slowly when the diet was properly altered Changes vary with age young individuals showing mild xerosis and adolescents manifesting greater evolution of follicular lesions (Frazier et al ADS 48 1 1943)

Phrynoderma to d skin) w common among the T m l f the Federated Malay States, Fasal ADS 50 160 1944) reported. M ny f hi patients showed Bitot spot white triangular lesion f the lateral sclera which probably are due t itaminosis. Red palm oil proved a heap and effect e source of vitamin A for these people



Fig. 443.



Fig. 444.



Fig. 445.

Figs. 443-445.—Avitaminosis A: clinical pictures of follicular hyperkeratosis of buttock and elbow and photomicrograph of follicular hyperkeratosis. (Frazier and Hu: ADS 33: 825, 1936.)

Acneform, comedo-like noninflammatory lesions were the feature of children studied by Youmans and Corlette (AmJMSc 195: 644 1938). Keratosis pilaris, lichen pilaris, lichen spinulosa, and ichthyosis follicularis seem merely different names for avitaminotic lesions in the opinion of Lehman and Rapaport (J 114: 396 1940). Response to vitamin A therapy in a dose of from 100,000 to 300 000 units per day requires to 4 months. Hecht and Mandelbaum (AmJPhys 130 651 1940) likewise found 6 weeks or more requisite to recovery from visual threshold defects. Nail changes in avitaminosis A comprise thinness and fragility, longitudinal ridges, transverse bands, and punctate pits, which ceased to appear in White's patients (J 10... 2178, 1934) when haliver oil was administered. Conjunctival folliculosis responds to vitamin A administration (Sandels et al.: AmJDisChild 62: 101 1941). See also Darier's disease. The use of vitamin A in acne (q.v.) is generally disappointing.



Fig. 586.—Avitaminosis A. (Drs. Frazier and Hu.)

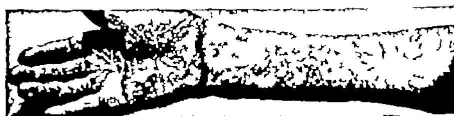


Fig. 587.—Pityriasis rubra pilaris. (Dr. J. B. Shelmire.)



Fig. 588.—Pityriasis rubra pilaris. (Dr. Howard Fox.)

Vitamin A depletion occurs in steatorrhea (Albright and Stewart, NEngJM 223, 239, 1940). It ... doubtful whether petrolatum laxatives cause deficiency (C... and Ballmer, J 113 1783 1939). Isaacs and Ju... g (PIMChi 12 ... 1940) could not detect it. Lacking vitamin A osteoclastic and osteoblastic activity is diminished, and the resultant dysplasia of bone produces grave effect on the nervous system, cranial nerves I, II, V and VIII suffering most (Mellanby, JPhys 105 382 1944).

Vitamin A disturbances often accompany thyroid dysfunctions ... the hypothyroid individual fails to utilize A and the hyperthyroid uses it excessively. Skin manifesta-

these are well described and illustrated by Platt (BritMBull 3: 179 1945). Vitamin A chemistry is discussed by Batt (J 120; 1030, 194 ) its synthesis by Milas (Sc 103: 581, 1946). Oral administration is simpler and probably even more effective than parenteral in the average case (Lease: JLCM 7 502, 194 ).

Hypervitaminosis A was shown by Toomey and Morissette (AmJDisChild 73: 473, 194 ) to have been the cause of oily scaly rough, itchy skin and painful swellings of the extremities, anorexia, constipation, and irritability of a young child.

Pityriasis Rubra Pilaris is a rare chronic, sometimes fatal disease characterized by hard, yellowish or reddish hyperkeratotic papules situated at the mouths of hair follicles and coil gland ducts. The nutmeg graterlike appearance of the baby aspects of the dorsa of the fingers is a classic feature. Dry scaling as in seborrheic dermatitis may cover much of the body in extreme cases. Cachexia and weakness develop.

The identity and nature of the disorder were for many years the subject of controversy but it apparently represents nutritional deficiency principally in vitamin A (Jeghers: NEngJM 228 714 1943; Pettler PaMJ 39 864, 1936; Werner and Levin: ADS 43: 289, 1943 Brunsting and Sheard: ib, 43: 4, 1941). Large doses of vitamin A help such patients though this is not the whole story, in the judgment of Porter and Godding (BJD 57: 197 1945) for liver function is probably deranged (Leitner: BJD 58: L( 1946). Familial cases were reviewed by Leitner and Ford (BJD 59: 407 1947) it being judged that the disease is inherited as a simple autosomal, heterozygous condition; some of their patients showed defective liver function.

**The Water Soluble Vitamins** include at least the following factors (Elvehjem J 120 1388 1942)

thiamine ($B_1$)—antineuritic
riboflavine ($B_2$ or G)—antiperleche and growth factor
niacin (P P nicotinic acid)—pellagra-preventive
pyridoxine ($B_6$)—rat antidermatitis factor
pantothenic acid (filtrate factor)—needed by all living things
biotin (H)—antiegg white injury factor
para-aminobenzoic acid—antigray hair factor
inositol—mouse antialopecia factor
choline—growth factor needed for formation of methionine
ascorbic acid (C)—antiscorbutic
citrin (P)—hesperidin and demethylated hesperidin (eriodictin) antihemorrhagic
grass juice and milk factors—essential for guinea pigs
L. casei factor (folic acid)—antipernicious anemia factor (Spies: J 130 474, 1946)

**Vitamin $B_1$**—In pellagra (q v ) administration of B relieves the neuritic element but does not influence dermatitis or stomatitis. (Williams and Spies Vitamin B Macmillan, 1938 )

**Vitamin $B_2$**—Is a complex this was formerly considered at least quadripartite including nicotinic acid riboflavin, a rat antidermatitis factor and a chick antidermatitis factor (Nelson J 110 645 1938)

Pantothenic acid and p-aminobenzoic acid (anti-gray-hair vitamin) are further members of the group The actual anti-gray-hair value of these when given for that purpose to human beings is highly dubious (Edit J 122, 875 1943)

B now designates riboflavin Its deficiency was clarified by Sebrell and Butler (PHRpts 54 2121 1939) who induced the condition experimentally and observed the development of a reddened denuded lesion of the lips, maceration and fissuring in the angles of the mouth, and seborrheic accumulations at the nasolabial folds These manifestations appeared after approximately 3 months and were curable and preventable by the administration of pure riboflavin Sydenstricker et al (J 113 1697 1939) confirmed these findings, and (J 114 2437 1940) described an additional feature comprising characteristic lesions of the cornea photophobia and dimness of vision not relieved by refractive correction burning of the eye

balls and roughness of the lids and extreme visual fatigue Circumcorneal injection progressed to superficial vascularization of the cornea, starting at the limbus, and riboflavin, 5 to 15 mg per day specifically relieved the condition This type of keratitis is, according to Sydenstricker et al. (SMJ 34 165 1941) the earliest and commonest visible manifestation, which had been noted in rabbits by Bessey and Wolbach (JExpM 69 1, 1939) Jolliffe et al. (NEngJM 221 921 1939) described filiform excrescences arising from the sebaceous glands of the face in skin areas showing a greasy fine desquamation Cheilitis and perlèche were also frequently present in their patients Riboflavin is valuable in rosacea (q v ) see also stomatitis, metabolic.

**Vitamin B₆ (Pyridoxine)** prevents an acrodynia like condition of rats, with alopecia of the paws and about the mouth. Its administration seemed occasionally helpful in various eczematoid conditions in which it was tried by Wright et al. (ADS 47: 651, 1943) A syndrome of itchy patchy superficial, vesicular and scaly erythroderma with macrocytic anemia was reported by Stryker and Halbeisen (ADS 51: 116, 1945) Lesions occurred on the face neck, and upper part of the chest and resembled pellagra, neurodermatitis or venenata. Improvement was usual when the patient received a good diet, pyridoxine, and injections of crude liver extract.

**Folic Acid** has been proved to be the *Lactobacillus casei* factor responsible for primary macrocytic anemia, and its administration in the crystalline form induces prompt increase in red blood cells, reticulocytes, and hemoglobin in such cases (Spies et al BMJ 39 707 1945) Parenteral and oral administration are equally effective in nutritional pernicious anemia and the macrocytic anemia of pellagra in a dose of 5 to 10 mg. by injection or 100 mg by mouth daily (Spies: J 130 474 1946) Loper et al. (J 132 906 1946) rehabilitated patients with sprue satisfactorily although the intestinal parasites were not altered. A case of pernicious anemia placed on folic acid showed response in the blood picture but serious neurologic relapse occurred despite the vitamin (Heinle and Welsh J 133 739 1947) A maintenance dose is about 5 to 10 mg. per day by mouth.

**Vitamin B₁₂** is a factor required by *L. lactis* present in refined liver extract in almost linear relationship to the unit potency of the extract in pernicious anemia (Shorb JBiolChem 169 455 1947) Crystallized (Rickes et al. Sc 107: 396, 1948) it produced hematologic response in 3 cases of pernicious anemia when given in single intramuscular doses of 36 to 150 micrograms (West: Sc 107 398, 1948) Spies et al. (SMJ 41 522, 1948) confirmed its value in Addisonian anemia and sprue with striking clinical improvement including an increase in feeling of well being, mental alertness strength, vigor and complete relief of soreness and burning of the mouth and tongue. The chemical is a red crystalline compound which contains cobalt phosphorus, and nitrogen, but not sulfur (Rickes and Koniuszy Sc 108 134 1948)

**Choline** is a component of the phospholipid lecithin and plays a role in the prevention of fatty livers in depancreatized dogs (El ehjem, 194_) Considered an important member of the B complex, its function is in some way related to the mobilization of fatty acid in the body serving perhaps to stimulate the formation of phospholipids, to make possible the production of acetylcholine or to supply labile methyl groups as methionine does (M Henry Choline, the B Vitamins and Fat Metabolism, Lancaster Pa., 1941) Its significance in dermatology unassessed

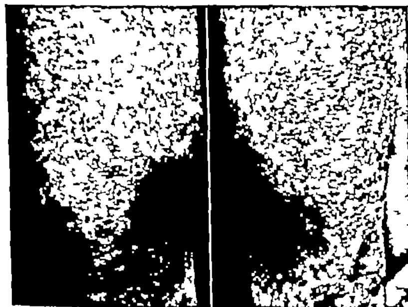
**Inositol** was shown by Woolley (Sc 92 384 1940) to be the factor responsible for cure of mouse alopecia.

**Vitamin P (Citrin)** has been found to consist of flavone components, hesperidin and eriodictin. It appeared to be concerned with the regulation of capillary permeability and fragility (Warren and Webb Sc 96 30_ 194_) and corrected fragility in scurvy cases in which ascorbic acid alone accomplished only partial cures (Scarborough Lancet 644 1940 EdiMJ 50 85 1943) The present 0 rgyi preparation proved inert however when purified and the hemorrhage preventive may actually be rutin (Edit BMJ 1 771 194_) See purpura (p. 431)

**Vitamin C** Purpuric lesions due to scurvy are due to capillary fragility and the tourniquet test shows that fragility is most marked in the perifollicular vessels Swollen gums, loose teeth and gingival hemorrhages are typical features.



Fig. [illegible].—Avitaminosis C gingival swelling which almost completely obscures the teeth and petechiae (Dr R. Staehelin.)



Figs. 530 and 531 —Avitaminosis C follicular petechiae. (Dr R. Staehelin.)

A man on a C-deficient diet did not develop petechiae until the 161st day and there was no demonstrable increase in capillary fragility; but he lost 23 pounds in weight and showed follicular hyperkeratosis of the buttocks and calves, and ascorbic acid given intravenously was promptly restorative (Crandon et al.: NEngJM 223: 353, 1940). Bleeding of the gums does not occur in scorbutic infants until after dentition (Jeghers: NEngJM 228: 19, 1943). The vitamin C concentration of the blood is related to the dietary intake but apparently good health may be associated with low values, according to Lever and Talbott (ADS 41: 65, 1940) who could detect no relation of psoriasis, urticaria, lupus vulgaris, lupus erythematosus, eczema, or purpura to the vitamin. Saturation may be estimated by determinations of urinary excretion of ascorbic acid after giving 600 mg. intravenously (Goldsmith and Ellinger: AIntM 63: 531, 1939). Wound healing, well being and complement titer are probably significantly related to adequacy of the vitamin C level (Ecker et al.: J 112: 1449, 1939) yet the utility of its administration in dermatology lacking such classic indications of its need as were described by Osterlin (JMichSMS 44: 1331, 1943) in scorbutic children is quite dubious.

In severe scurvy bloody tumors of the conjunctiva and ecchymoses of the lid and elsewhere about the eyes may appear but degeneration of the cornea, pigmentation and night blindness, once reported due to avitaminosis C, are now known to be the results of lack of vitamin A. Perifollicular or petechial hemorrhages characteristic of scurvy are commonest on the lower extremities, where pressure exposes the weakness *of the capillaries. Vitamin C is cevitamic acid. It may be given intravenously in large* doses and may diminish reactivity to arsenicals (Cornbleet: JInvD 4: 81, 1941).

**Vitamin D**.—Cod liver oil is a rich source of the antirachitic vitamin. We have seen epidemics of acne caused by its wholesale administration to groups of children. The effect of the oil in causing acne (q.v.) is due we presume to the malmetabolism of provitamin A. Vitamin D concentrates, such as ertron and calciferol, have utility in the treatment of lupus vulgaris (q.v.) and psoriasis, perhaps. The lack of vitamin D does not produce cutaneous symptoms.

**Vitamin E**, of which wheat germ oil is a rich source, is essential to the successful completion of pregnancy and to lactation. Without it the male testis becomes sterile. Alpha tocopherol is a crystalline substance of potent vitamin E activity (Evans et al.: JBiolChem 113: 319, 1936) synthesized by Karrer et al. (HelvChimActa 21: 520, 1938) a plausible dose of which is 3 mg. per day. No harm has come of much larger doses, although an occasional idiosyncrasy such as pruritus or urticaria has been reported (Shute: AmJOG 35: 249, 1938). It may be useful in some cases of *pruritus vulvae* being antagonistic to estrogen. Necrobiosis lipoidica responded favorably, also several cases of lupus erythematosus, reported Burgess (TransA.D.A. 1947) and Anderson in discussion pointed out its influence on fat metabolism and collagen and indicated its possible utility in poikiloderma, arthritis, Dupuytren's contracture and knuckle pads.

**Vitamin F**, comprising the unsaturated fatty acids (linoleic, linolenic and arachidonic) necessary for the rat, preventing scaly dermatitis, is of unknown significance to the human being (Finnerud: ADS 44: 849, 1941). See eczema, atopic; also Hansen and Burr: J 132: 855, 1946.

**Vitamin G** is known as $B_2$, riboflavin.

**Vitamin H** (Biotin, according to du Vigneaud et al.: Sc 92: 62, 1940) is a growth factor needed by many bacteria and molds and most animals (Edit.: BMJ 2: 655, 1943). Deficiency is produced by adding raw egg white to the diet which inactivates it, or by feeding sulfonamides which interfere with the bacterial synthesis of it. Thinning of fur in monkeys, alopecia, and scaly dermatitis especially of the face and extremities were produced by withholding the nutrient by Waisman et al. (JNutrit 26: 1, 1943). Human volunteers on a diet free from biotin, poor in all vitamins except riboflavin and rich in egg white, developed a fine scaly nonpruritic dermatitis within a month under the observation of Sydenstricker et al. (J 118: 1199, 194 ). They also

manifested reticulation of the extremities depression, lassitude anorexia, muscle pains, and hyperesthesia. The syndrome was curable by the administration of 150 to 300 μg of biotin daily

Vitamin K is an antihemorrhagic factor which shortens a prolonged prothrombin time. Richly present in alfalfa, its isolation, chemical constitution, and synthesis were described by Doisy et al. (Sc 90: 407 1939) see also Snell and Butt (J 113 2056 1939) It has been used successfully in some cases of purpura (q v) for in its deficiency ecchymoses and suffusions especially over pressure sites, rather than dependent ones, may cover large areas of skin (Kark et al.: QJM 9: 247 1940)

Vitamin L, a liver extract lactation factor for rats, is similar to the filtrate factor W and is of dubious status (Edit. BMJ 1 196 1940)

*Vitamin M is a dubious member of the B complex in liver extract.* Its deficiency in the monkey produced glossitis and symptoms of sprue and was restored by injections of purified *L. casei* factor (Day et al. Sc 103: 108, 1946) so that it may actually be folic acid.

**Treatment.**—The treatment of the avitaminoses is direct and satisfactory It is better to err on the side of excessive dosage, for overdose symptoms are rarely conspicuous. Many of the cases one sees are persons of limited means and understanding but they are capable of being taught to spend a meager food allowance more to their profit. Appropriate vitamin therapy may be depended on to relieve avitaminosis it is no panacea. Hydrochloric acid is generally advisable if the B complex is to be prescribed (Allison SMJ 38 235 1945) Half of an orange a day promptly cures the scurvy we see in our dispensary work. A pork chop is a rich source of vitamin B Pellagra must be recognized, and its efficient treatment is inexpensive and satisfactory Spoon nails and smooth tongue in an anemic middle-aged woman with dry lusterless hair and a notably acne free complexion call for nutritional therapy It has been hard to see through the murk of faddism even among alleged nutritional experts, but creditable investigators of genius and persistency are clarifying the scientific problems, and science eventually reaches the public If presumptive hypovitaminosis is wholly subclinical we think it is for practical purposes insignificant.

## PELLAGRA

**Symptoms.**—This avitaminotic symptom complex represents deficiency in the B factors Degrees of severity are widely divergent the classic designation of the extreme case being given by the four D s, dermatitis, dementia, diarrhea and death Since several vitamins, rather than one are usually simultaneously deficient and the relative inadequacies of each may be different and the causes of deficiency may differ the variety of manifestations embraced by the connotation of pellagra is considerable. Typical symptoms include *gastrointestinal and neurologic* disturbances accompanied by dermatitis, pigmentation and photosensitivity

Cutaneous lesions generally affect the dorsa of the hands, wrists, and feet and the face and neck. The eruption is generally symmetric Early changes are large inflammatory macules which coalesce to form patches resembling sunburn. Desquamation ensues, and a rough, scaly surface results. In acute and severe examples, bullae may form and these are likely to become secondarily infected. Sunlight influences the location of lesions. These may also be determined by stasis, scars, injuries, burns, friction and inflammation and relapses may be induced by heat and ischemia (Bean et al. ADS 49 335 1944) so that the lesions are not always symmetric

Cheilitis and stomatitis are expected and colpitis and vulvar dermatitis are common. Monilial infection of such subnormal mucosae is usual the



Fig. [illegible].



Fig. [illegible].

Fig. [illegible].—Pellagra: dermatitis of exposed skin. (Drs. [illegible] and T. Twyman.)

Fig. [illegible].—Pellagra. (Dr. O. L. Castle.)

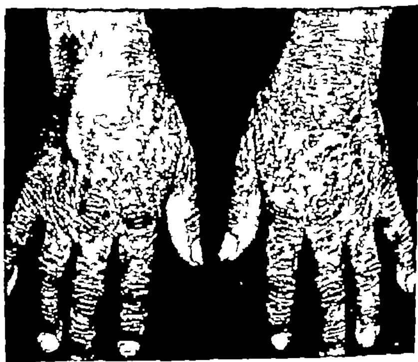


Fig. [illegible].—Pellagra. (Dr. Grover Wende.)

monilia disappearing when vitamin replacement therapy is adequate. Vaginitis and proctitis correspond in severity to the stomatitis. The tongue is swollen, red dry denuded and perhaps superficially ulcerated

Diarrhea is not invariably present, but there may occur constipation, perhaps alternating with diarrhea. Emaciation and weakness correspond in the main with the severity of gastrointestinal symptoms. Anemia, diminished blood protein and dependent edema may occur Neurologic manifestations include toxic psychosis, confusional or even maniacal and polyneuritis, loss of reflexes and paresthesias.

Exposure to sunlight may precipitate pellagrous dermatitis in susceptible subjects (Smith and Ruffin AIntM 59 631 1937) Acute onset may be manifested by confusion and sore tongue (Gottlieb BMJ 1 392, 1944) and the postoperative period, especially after gastrointestinal surgery may be the occasion of the appearance of pellagra. Psychoses of the senile type with memory defects and episodes of stupor accompanied by mucosal changes of avitaminosis, are sometimes attributable to pellagra (Meyersburg NEngJM 233 173 1945) Lesions characteristic of the disease are seldom seen in infancy but in endemic areas the dietary histories of the mother and infant and the response to the administration of specific therapeutic agents make the diagnosis (Spies et al J 113 1481 1939)

Purpura, linear in configuration, resulting from scratching and not related to vitamin C sometimes [illegible] a symptom of pellagra (Simons and Simons BMJ [illegible] 817 1946)

Atypical cases have been described by Smith et al. (JIn D 4 [illegible]3, 1941) wherein dyssebacia is seen, with dry flakiness of the face and plugged sebaceous follicles, features now recognized as mainly due to ariboflavinosis or hyperkeratosis over the pressure site ichthyosiform alterations swelling of the tongue paresthesias, and loss of energy may comprise the picture (Field et al NEngJM 223 307 1940) Nondescript stomatitis and glossitis in patients in mental hospital were actually pellagrous, reported Evan (BMJ 6 439 1939) Unusual locations of the dermatitis such as submammary and vulvar but reviewed Riordan et al. (ADS 46 661 194 )

Deficiency dermatitis of the scrotum occurred in prisoners of war in the Far East (Frankland; BMJ 1 1023, 1948) Irritation was worse at night. Exacerbations were promoted by hard work, heat and intercurrent illness. Clinical varieties included a mild type a severe dry and fissuring type chronic maceration with fetor, and an ulcerative and edematous type Associated oral lesions resembled ariboflavinosis. Also were seen retinal atrophy and painful burning feet

Diagnostic problems, atypical and borderline cases were discussed by Gross (ADS 43: 504 1941) and Spies et al. (J 126 3[illegible] 1944) X ray examination of the gastrointestinal tract may reveal dilation and slow emptying of the stomach, atrophy of the mucosa and gas in the gut (Rubin and Bohlan [illegible] J 4 408 1942) The electrocardiogram may show sinus tachycardia, alteration of the ST interval and of the T wave and low voltage but no characteristic feature (Mainzer and Krause BHeartJ [illegible] 83, 1940)

The course of the chronic disease is variable It generally becomes manifest in the summer or early fall lasting a month or more Dermal symptoms may recur during several successive summers. Neurologic changes are seldom demonstrable in mild cases, but sometimes comprise the conspicuous or even the sole findings Mental symptoms and peripheral neuritis are attributable to the lack of B

**Etiology and Pathology**—No age or class of persons is exempt although elderly people of poor economic status are the usual victims. The endemic regions in the U.S.A are characterized by a population with a high proportion of persons whose economic circumstances are substandard and whose diet includes a good deal of maize. But pellagra

occurs in anyone in whom the ingestion, absorption, or utilization of the essential nutrient factors is inadequate (O'Leary NoWM 27 319 1928) The alcoholic senile or mentally defective individual failing to nourish himself decently is subject to pellagra Anatomic interference with gastrointestinal function and absorption may be causative. Intestinal parasites or other debilitating circumstances may tip the balance unfavorably when the supply of the required vitamin is borderline.



Fig 595 —Histology of pellagra, showing superficial inflammation, epidermal atrophy and irregular hyperkeratosis. (Moore et al, ADS 46 100 1942.)

**Specific Pellagra-Preventive Factor**—Red meat and yeast are foods which will prevent and cure both pellagra and the Goldberger type of canine blacktongue, which is the true analogue of human pellagra. While Funk (J 109 2096, 1937) had isolated nicotinic acid in 1911 while trying to isolate vitamin B from yeast and rice he found it inactive in curing polyneuritis in pigeons and investigated it no further It was Elvehjem and Madden (E 86 1, 193 ) who observed that nicotinic acid amide cures blacktongue in dogs. Smith et al. (J 109 2054 1937) cured the first human pellagrin whose diet was deficient in the preventive factor with pure nicotinic acid. Nicotinic acid cures glossitis but it does not relieve neuritis; vitamin $B_1$ does relieve neuritic pain. Spies et al. (J 110 [illegible] 1939) found that a dose of 100 mg given by mouth 3 times a day is safe and effective it can be given intravenously in doses of 50 mg twice daily but must be given slowly to avoid severe vasodilator reaction. Nicotinic acid is 3 pyridine carboxylic acid See Elvehjem (PhysRev 20 249 1940)

Niacin intake is not the whole story in pellagra. The intestinal flora in man produce and release nicotinamide in consequential amounts; the significance of this is discussed by Ellinger (J 130 668, 1946) Krehl et al. (Sc 101 489 1945) showed that tryptophane prevents deleterious effect of corn in the diet it being previously known that corn ingestion increases the niacin requirement (Edit J 129 73 974 1945) Overingestion of adenine produces pellagra in dogs, and a relationship exists between purine metabolism and avitaminoses according to Raska (Sc 105 126, 1947)

Porphyrinuria is not constant in pellagra and is not the explanation of the photosensitivity (Kark and Meiklejohn AmJMSc 201 380 1941); see also porphyria. When present, it depends perhaps on altered hepatic function. A extract of the liver of a pellagrin who died effected blood regeneration in a patient with pernicious anemia

but did not benefit other pellagrins, whose subsequent responses to commercial liver extract was favorable (Sydenstricker et al.: AmJMSc 197: 755 1939) The pellagrin manifests abnormal sensitivity to insulin, as does the sufferer from Addison's disease responding to small doses with deep and prolonged hypoglycemia (Mainzer abs. J 113: 986, 1939)

Histologic changes in pellagra are dyskeratotic and inflammatory but nonspecific and are reversible under appropriate treatment (Moore et al. ADS 46: 100 1942)

Treatment.—Patients with acute pellagra are well treated by nicotinic acid in doses of 50 mg given 10 times a day by mouth even if vomiting occurs. The fiery redness and swelling of the tongue fade within 24 hours of the commencement of specific therapy salivation and oral discomfort promptly diminish, Vincent's infection heals quickly and erythematous skin lesions blanch rapidly Nicotinic acid is not a substitute for a full, balanced diet. Nicotinamide does not cause the vasodilation that niacin does, and so may be given intravenously The requirement for cure is about 100 mg t.i.d. Adequate amounts of the whole B complex should be assured in any patient, for it is unlikely that niacin alone is deficient. A liberal and well-balanced diet must be urged.

## NUTRITIONAL EDEMA

Gross malnutrition and starvation, such as have occurred with distressing frequency among children of war torn region and some prisoners of war result in a syndrome of emaciation faintness, asthenia, anemia, bradycardia, hypotension, paresthesias, diarrhea, and polyuria. Cutaneous atrophy occurs, with wrinkling, scaliness, and pigmentation especially of the hands, legs, and face. Mucosal involvement, including even ulceration may develop, resembling severe pellagra. Dependent edema appears in such persons suddenly Scabies, impetigo, abscesses, ulcers, and keratosis pilaris are common. Jiménez et al. (abs J 122 140 1943) reported such cases from Spanish civil war experience and he found blood and plasma transfusions beneficial. Ortiz (abs J 115 1929 1940) described similar findings in Puerto Rican children, where diarrhea and general debility responded to high protein diet, vitamins, iron, and transfusions. Apathy and complaint of pain on passive motion, a swaying gait in those who could manage to walk, and photophobia, alopecia, and acrocyanosis were features of the starved infants described by Chavarria and Rotter (abs ADS 59 659 1939) Starvation phenomena were reviewed by Keys (J 138 500 1948)

Kwashiorkor is the South African name for what seems to be the same condition, an infantile pellagra which is rapidly fatal, associated with fatty degeneration of the liver and the development of curliness and depigmentation of the hair (Gelfand ClinProcCapeTown 5 135 1946) The Gillmans (J 129 12, 1945; Lancet 2 446, 1946) finding this African syndrome not responsive to diet vitamins, and liver extract, gave dried hog stomach with success; Ventriculin 10 gm. per day and HCl by mouth were spectacularly effective.

## PLUMMER-VINSON-SJÖGREN SYNDROME

Hypochromic anemia, dysphagia, glossitis, and achlorhydria are the features of this disorder which occurs in middle aged and older women. The lips are thin and the opening of the mouth is small and inelastic Andrews wrote (Dis. Skin Saunders, 1946) and atrophy is most pronounced on the tongue which in typical cases is entirely smooth, but there are associated atrophic changes in the mucosa of the mouth, pharynx and esophagus. Inflammation is also present the lips may be swollen and crusted, and the tongue enlarged, tender and bright red. Dysphagia may resemble hysteria (Vinson MinnMed 5 107 1922). It may be due to painful pharyngeal and esophageal lesions, where hyperkeratosis and atrophy suggestive of vitamin A deficiency are troublesome The mucosa is thin, may even be lacerated (Kernan AOtol 32: 662, 1940) Filiform keratitis is the ocular manifestation featured by Sjögren's contribution; this and the cheilitis suggested ariboflavinosis to Franceschetti (abs J 122 713 1943) Dysphagia, weakness, brittle nails, and iron depletion were accurately described by Dammerbek (J 100 540, 1940) Patterson (1919) and Kelly (1919) were accredited

with priority by Morrison (J 114: 512 1940). Stagnation of barium in pharyngeal pockets above the laryngeal aditus may be found fluoroscopically (Gerlings: JLaryng 55: 148 1940). Xerostoma from hypkeratosis not uncommonly progresses to leukoplakia and squamous carcinoma which, when it occurs in the pharynx and esophagus of women, is often the result of this syndrome (Ahlbom: BMJ 2 331 1936). Koilonychia is a usual feature, too. Anderson (ADS 37 816 1938) emphasized. In treatment, hydrochloric acid, iron, and vitamin concentrates, especially B complex and vitamin A appear indicated, while esophageal dilation may be required, and the mechanical as well as the *nutritional qualities of the ingesta must be considered. Since* vulvar changes in kraurosis resemble those of the pharynx in this syndrome estrogen in suitable dosage might not be amiss.

## KERATOSIS FOLLICULARIS

**Darier's Disease** is a rare dermatosis characterized by a symmetric eruption of small firm papules which are reddish at first but become darker and enlarge to form papillomatous growths. Lesions occur on the



Fig. 396



Fig. 397

Fig. 396.—Darier disease. (Dr Bedford Shelmire.)
Fig. 397.—Darier disease. (Drs Stevens and Fisher.)

sides of the forehead and neck, the nape of the neck, over the shoulders and along the midline of the trunk by predilection. When a crust is removed, a minute funnel-shaped depression is left in the top of a papule. The lesions are at first discrete but tend to become confluent. On the scalp masses of oily crusts are comparable with those occurring in severe seborrheic dermatitis, and alopecia may result (Welton ADS 47 398 1943). As a result of fermentation, they may suppurate or ulcerate and emit a highly offensive odor. About the genitalia and the anus the lesions may vegetate. The health is little involved, but the victim may be prevented by his disease from earning a living. Cases range in severity from mild to extreme.

**Etiology**.—The cause is not known. Two or more cases may occur in the same family (Hitch et al SMJ 34 678 1941) and inheritance is transmitted through and to both sexes as an irregular dominant character The relationship to disturbed vitamin A metabolism was recognized by Peck et al., who reported (ADS 43 223 1941) colorimetric studies of blood serum concentrations of A indicating that low values exist in patients on



(Dr D. B H Cleveland.)

Fig. [illegible].—Darier's disease mild, showing verruca-like lesions scattered about neck.





Figs [illegible] and [illegible].—Darier's disease histologic structure. Note hydropic change in stratum mucosum, intraepidermal [illegible] left, hyperkeratosis and [illegible]. (Dr Fred W [illegible].)

normal diets. Later studies (Peck et al. ADS 48 17 1943) showed correlations of dark adaptation and low vitamin A values in the serums of 8 of 10 patients. Unless large amounts of A were supplied, the serum levels would drop. Carleton and Steven (ADS 48 143 1943) tested 4 patients and found no evidence of vitamin A deficiency yet 2 of their patients responded favorably to its administration.

**Pathology.**—Acanthosis and disruptive loss of cohesion between the basal epidermal layers are typical. In the depths of the lesions are peculiar hyaline, doubly-contoured bodies representative of degenerated epithelial cells (Pels and Goodman ADS 39 438, 1939). The dyskeratosis seldom affects a hair follicle, though slitlike orifices filled with loose keratinized material are seen at the depths of the interfollicular epidermis and sometimes at the sides of follicles (Ellis ADS 50 27 1944). Compare familial benign pemphigus. Histologic examination differentiates acanthosis nigricans and other possibly confusing disorders.

**Treatment.**—Vitamin A in a dose approximating 200 000 units per day is often remarkably helpful. Its utilization may be enhanced by giving hydrochloric acid also, and perhaps thyroid. Vitamin A therapy of 100 000 units per day is adequate and should not be abandoned in less than 2 months, though it helped not at all in 2 of 7 cases of Porter et al (ADS 56 306, 1947) who found vitamin A ointment without value. Locally in mild cases the generous use of zinc stearate powder is comforting, or an ointment containing 1 to 2 per cent of salicylic acid or resorcinol. X ray therapy affords fairly effective palliation, grenz radiation being of especial value because of the need for inducing epidermal atrophy and the desirability of harming the dermis as little as possible.

# DERMATOSES OF VASCULAR ORIGIN PURPURA AND VASCULAR GANGRENE

## PURPURA

Purpura designates hemorrhage in the skin and mucous membranes, manifested by an eruption consisting of petechiae which are visible hemorrhagic reddish or purplish macules. Their blood color does not disappear under diascopic pressure. In time the lesions resolve undergoing the color changes seen in bruises. Hemoglobin becomes hemosiderin, is phagocytosed and eventually carried away. Purpura can occur either by diapedesis or by rhexis of the vessel wall. Blood deep in or beneath the skin is likely to appear purple rather than red. A purpuric eruption is a symptom of a vessel-damaging disorder which may be fairly well understood, in which case the purpura is called *symptomatic* or which may be classifiable but ill understood, in which case it is called *idiopathic*.

**Symptomatic Purpura.**—Cutaneous hemorrhages may occur in typhus, meningitis, typhoid fever, scarlatina, measles, smallpox, septicemia, bacterial endocarditis, plague, exophthalmic goiter, scurvy, spirochetal jaundice and acute yellow atrophy. Petechiae in bacterial endocarditis often have white centers. Purpura may appear in chronic nephritis, heart disease, pernicious anemia, tuberculosis, starvation, leukemia, pituitary basophilism, aplastic anemia, periarteritis nodosa, severe cough, and other disorders. Bites may be purpuric or may provoke purpura—purpura pulicosa is that due to fleas.

**Allergy** in relation to purpura was discussed by Thomas and Forsythe (JLCM 26 1103, 1941). Of 10 of 64 patients with hemorrhagic purpura a family history of allergy was found in 8, thrombopenia in –, and allergic manifestations of one sort or another in all. An inhalant was shown to be the cause in 1 case and foods in another. Necrotic purpura occurs in rare instances, the resulting cicatrices having an artificial appearance; it may be related to the Shwartzman phenomenon (Sheldon: ADisChild –1 7 1947).

**Avitaminosis and Purpura.**—Lack of vitamin C (q.v.) results in increased fragility of vascular endothelium. Vitamin P (q.v.), a crystalline flavone found associated with C but distinct from it, was observed to control purpura when vitamin C did not (Jerold: Lancet 1 1443, 1939). Vitamin K (q.v.) is curative in hemorrhagic disease of the newborn, a disease characterized by hematemesis, melena, hematuria, cerebral symptoms and dermal hemorrhages (Poncher and Kat: J 115 14 1940).

Rutin is the crystalline flavonal glucoside of quercetin derived from buckwheat. The relationship of this nontoxic substance to vitamin P (q.v.) was discussed by Shanno (AmJMedSc 211 539 1946) and its value in hypertensive patients observed. Its influence on capillary fragility in doses of 20 mg by mouth t.i.d. was reviewed by Zfass (VaMMonth 74 56, 194 ). Those at ... proved responsive and retinal hemorrhages in hypertensive patients subsided.

**Cullen's Sign.**—Blood staining at the umbilicus generally is due to ruptured ectopic pregnancy; it may signify any intraperitoneal hemorrhage.

**Hemophilia.**—Purpura, ecchymoses, epistaxis, and menorrhagia are common.

**Mechanical Purpura.**—In some persons petechiae may appear following slight trauma, or even as a result of gravity.

**Meningococcic Purpura** and dermatitis are considered on p. 190. Fulminating adrenal hemorrhage sometimes meningococcic in etiology and sometimes of unknown cause is a catastrophic illness, generally fatal, in which the abrupt onset with fever, nausea, vague abdominal pains, headache, and restlessness are soon followed by lilac cyanosis, shock, and generalized petechial rash which spreads rapidly. Peripheral circulatory failure ensues and the course of this Waterhouse-Friderichsen syndrome

is run in 8 to 24 hours. Pratt Thomas et al. (BMJ 38 229 1943) described 4 cases with 1 recovery attributed to prompt diagnosis and administration of sodium sulfadiazine intravenously. McLean and Caffey (AmJDisChild 4 1033 1931) found meningococci in skin smears in 86 per cent of their cases. Oxygen, adrenal cortex extract, and plasma were also helpful in a patient of Johnson (ADS 5 391 1943).

**Menstrual Purpura.**—The rash generally involves the dependent parts and is symmetric, recurrent and associated with scant menstrual flow. Corpus luteum treatment may help such cases (Stöge KlinWchs 56 770 1942).









Figs. 401-404.—Purpura.

**Nervous Purpura.**—Purpuric spots may follow severe fright, and also possibly various neuropathic influences. Remarkable bleeding at gums have occurred in religious ecstasy (Klauder ADS 37 650 1939).

**Purpura Rheumatica**, the peliosis rheumatica of Schonlein, is purpura simplex associated with arthritis or erythema of rheumatic fever (q v ); Scheel (abs J 119: 1147 1942) obtained rapid subsidence by giving vitamin K.

**Senile Purpura** occurs in elderly individuals and commonly affects the legs, arms, and backs of the hands.

Solar Purpura.—Uncovered areas of blond, young, dermographic skins suffered purpura after exposure to sunlight, as reported by Berlin (abs ADS 40 815 1939). Pressure on the fingernail evoked subungual petechiae in these Scandinavian patients, who, despite xerosis, freckles, and telangiectases, appeared not avitaminotic.

Toxic Chemicals causative of purpura include iodides, snake venom, mercury, antipyrine, chloral hydrate, copaiba, benzol, arsenicals, phosphorus, quinine, sedormid, ergot, turpentine, belladonna, and salicylates.

**Idiopathic Purpura** may be thrombocytopenic or nonthrombocytopenic.

**Thrombocytopenic Purpura** includes cases called purpura hemorrhagica (morbus *maculosus* of Werlhof) which is a severe and sometimes fatal type with extensive hemorrhages into the skin, mucosae and viscera affecting chiefly young girls. The duration of purpura hemorrhagica is from 4 to 10 weeks, although chronic cases are seen with repeated attacks over many years. The onset is usually in childhood. Severity is variable but repeated, frequent attacks indicate the advisability of splenectomy (Vaughan and Wright J 112 2120 1939). Severe cases require splenectomy which probably removes a factor inhibiting maturation of thrombocytes (Limarzi and Schleicher J 114 14 1940). Transfusions, high protein, high vitamin diet, elimination of infections, viosterol, iron, and ultraviolet light irradiation were also recommended by Jones and Tocantins (J 100 83 1933).

Thrombocytopenic purpura is characterized by diminution in number of platelets, a critical level of which may be set at 60,000 per c mm., below which hemorrhage may be expected. The bleeding time is prolonged, the clot is soft and nonretractile and capillary resistance is decreased (Nygaard et al. PSEMC 15 753, 1940). While the clotting time is normal, there is delayed retractility of the clot. There is no morphologic change in the blood cells, and regeneration is normal.

Of 75 cases studied by Frans and Perry (Lancet 2 410 1943) 30 were of prepubertal age, of these 10 recovered spontaneously, splenectomy succeeded in 5 males and failed in 4 females, and mortality was 16 per cent. Of the 45 postpubertal cases, 38 were women, only 1 recovered spontaneously, splenectomy succeeded in only 7 of the 13 women who underwent it, and mortality was 40 per cent. Half of the deaths were due to subdural hemorrhage. One patient showed striking improvement during pregnancy. Thyrotoxicosis was associated with purpura in 4 cases. Splenectomy was successful in a woman 8 months pregnant reported by Polowe (J 124 771 1944). Splenectomy must be reserved for the idiopathic cases in adults, being a last resort in children and never used in symptomatic purpura.

Multiple platelet thrombi characterized the unusual and rapidly fatal acute febrile disease of a girl studied by Singer et al. (Blood 2 542, 1947) who found 11 similar cases of thrombotic thrombocytopenic purpura in the literature.

**Nonthrombocytopenic Purpura** includes cases of purpura accompanied by articular and visceral symptoms despite the absence of pathologic changes of the blood. **Henoch's Purpura** is of this type, a disease usually of early years, characterized by recurrent attacks of purpura sometimes accompanied by colic difficult to distinguish from the surgical abdomen, hematemesis and melena. Urticaria and erythemas are also seen, and edema of face, hands, and feet, as in Hadley's patient (Maine MAJ 33 184 1942). Confusion with surgical conditions is exemplified by the patient of Bisson (abs J 126 524 1944). The exanthem was largely depend-

ent in the 28 cases of Berggreen (abs YBD 1941 p 131) Food allergy may cause these phenomena (Hampton JAllergy 12 579 1941)

Treatment is to some extent empirical, accompanied by careful search for possible causes, including allergic ones. Vitamins C K and P may be tried and moccasin venom rutin and the antihistamine drugs. If the granules of the neutrophile polymorphs stain violet rather than blue it is not likely that a pyogenic infection is present. Transfusions and irradiation of the spleen may be tried (QMN J 119 918 1942 124 609 1944)

**Hereditary Familial Purpura Simplex** was described by Davis (Lancet 1110, 1939; 2: 441, 1941) from his observations of 27 families in which 88 members showed spontaneous ecchymoses and 84 of these were females. The 85 purpuric persons comprised 79 with purpura simplex, 4 with Schönlein's type with Henoch's, with easy bruising, and 1 with pseudohemophilia Of the 85 persons, 23 gave a history of rheumatic fever, 8 of rheumatoid arthritis 15 of some other form of arthritis and the others severe fibrositis. Platelet counts, bleeding time coagulation time fibrinogen, and clot retraction determinations were normal where tested.

**Etiology and Pathology**—Purpuras were reviewed by Peck et al (ADS 35 831 1937) who classified them as proposed by Rosenthal (JLCM 13 303 1928) with modifications related to the response to moccasin venom *Thrombocytopenic* idiopathic or secondary to leukemia aplastic anemia, pernicious anemia splenomegalic cirrhosis, Banti's syndrome Gaucher's disease and bacterial endocarditis or to drugs such as Sedormid arsenicals gold chrysarobin and *Nonthrombocytopenic* in Schönlein's and Henoch's types, nitrogen retention, endocrine disorders, hemophilia, jaundice and systemic parasitism such as meningococcemia, smallpox, and syphilis or in nutritional disturbances or in associated dermatologic conditions such as Majocchi's disease. While hyperactivity of the spleen in destroying platelets is one hypothesis regarding etiology supported by the benefits of splenectomy other authors suspect that the cause lies in the bone marrow in view of the fact that such agents as benzene x rays, bacterial toxins, and neoplastic metastases produce a reduction of platelets (Rittershofer OhioSMJ 44 154 1948)

Kracke (SMJ 34 56 1941) classified them in a practical manner in types characterized by (1) coagulation defect, due to defect in fibrinogen, calcium, or prothrombin; (2) platelet defect due to inadequate formation or excessive destruction; and (3) vascular defect due to malnutrition intoxication or allergy Investigation of any case should include (1) complete blood count ( ) platelet count (3) coagulation time (4) bleeding time (5) tourniquet test (6) clot retraction test (7) prothrombin clotting time and (8) plasma fibrinogen estimation if possible

The grouping which seemed appropriate for 153 cases studied by Rosenthal (J 11 101 1935) comprised (1) Acute cases, idiopathic or associated with infection or with drug idiosyncrasy, a type in which good results followed all forms of therapy splenectomy being inadvisable until the disease is proved chronic; ( ) Acute severe cases with fever and leucocytosis, perhaps with retinal and cerebral hemorrhages, a type generally refractory to all forms of treatment possibly showing severe reaction to venom (3) Cases with diminution in giant cells of the bone marrow a type manifesting severe reaction to venom (4) Chronic purpura a type showing variability in severity sometimes refractory to treatment and sometimes responsive to venom, often requiring splenectomy good results being generally obtained in cases in which a persistently positive venom reaction followed by splenectomy and some patients recover from the operation but continue to manifest purpuric symptoms.

In chronic hemorrhagic stimulation of the bone marrow occurs, with myeloid, erythroid and megakaryocytic hyperplasia and in this disease the megakaryocytes are of the young form while platelets are reduced in the marrow as well as in the peripheral blood (Limarzi and Schleicher J 114: 14 1940) In differentiation from leukemia, aplastic anemia and pernicious anemia bone marrow studies are of diagnostic value (Wiseman et al J 115 8, 1940)

In some purpuras vessel walls are apparently affected by some circulating toxin. Capillary fragility tests (q v ) of the tourniquet suction, or snake venom type may be applied and repetitions of their use may give an idea of the progress. Peck used 0.1 c.c of 1.3 000 moccasin venom intracutaneously which may provoke local hemorrhage in an hour change from positive to negative reaction is evidence of improvement.

**Prognosis** depends on the type of purpura present and what may be done about it.

**Treatment.**—Rest in bed is essential in all but mildest cases. Transfusions are to be considered, and sulfonamide intravenously is essential in the fulminating type Careful study is required to elucidate etiology and to define the purposes of treatment Calcium chloride and calcium lactate have been recommended In cases complicated with arthritis, the salicylates should be tried. One may give frequent small transfusions, a diet high in protein and vitamin content, viosterol and iron and ultraviolet irradiation Peck found repeated small doses of snake venom were followed by diminution in capillary fragility in many types of the disease but not in hemophilia. In thrombocytopenic purpura, splenectomy is usually indicated. This is not specific treatment, and recurrence may follow operation but, while being the most radical method, this is also the most effective Parathyroid extract has been used to obtain hypercalcemia. A low platelet count may sometimes be raised by injections of anterior pituitary hormone.

## DERMATOSES WITH PURPURIC MANIFESTATIONS

**Purpura Annularis Telangiectodes (Majocchi)** is a rare type of purpura characterized clinically by the development of punctate sharply defined, rose or red colored macules composed of dilated capillaries symmetrically distributed over the legs and dorsal surfaces of the feet and occasionally on the thighs, forearms, and trunk (MacKee: JCutDis 33: 129 180, 281 1915) Wise (JIn D 5 153 1942) described the lesional features authoritatively In the earliest stages the color of the lesions is bright red gradually assuming a darker red tint. Individual lesions may be linear macular stellate or serpentine; annular lesions are sometimes conspicuous but may be absent Brownish hyperpigmentation often haloes ringed lesions or appears in scattered spots independent of megascopic vascular lesions. Later atrophy may or may not become apparent. The rather abrupt formation of capillary ectases occurs without prodromal symptoms usually appearing in showers The dilated capillaries undergo evolutional changes, some remaining, others becoming thrombosed, still others perhaps rupturing. There is never palpable infiltration. The little red macules enlarge peripherally and merge with one another The central portions are likely to involute with atrophic cicatrization. The eruption is usually bilateral and symmetric and recurrences and relapses are the rule Itching is mild or absent Cardiovascular endocrine or other constitutional diseases of varied nature are commonly also present Histologic changes do not affect the epidermis, but just beneath it the vessels are dilated, some showing aneurysmal distortion, and blood detritus and iron pigment are scattered in the subcutis Small cell infiltrations, more abundant about widely dilated vessels are evidence of perivascular inflammation In late stages melanin pigmentation may be found Infiltration is replaced by atrophy and obliterating endarteritic vessel changes appear Effective treatment has not been reported

**Schamberg's Progressive Pigmentary Dermatosis** is a chronic disorder which begins with pin-head sized reddish points or dots forming irregular patches, which slowly extend by the formation of new lesions about the periphery The puncta in the course of time disappear leaving a brownish, brownish yellow or reddish brown pigmentation, which slowly fades. Spontaneous involution occurs in the oldest areas, and subjective symptoms are absent (Schamberg BJD 13 1 1901) Wise (JInvD 5 153, 1942) stated that annular formations and serpentine capillary lesions do not occur; that lichenoid and desquamative changes are secondary that hypercholesteremia is found in many of the patients who nevertheless appear to be in good health; and that there is no relationship between Schamberg's disease and varicose veins. His-

tologically the epidermis may be normal or hyperkeratotic parakeratotic and hyperpigmented. The subepidermal, papillary and subpapillary cutis contains cellular infiltrates in groups and band forms, more pronounced about the vessels of the appendages. The infiltrating cells are small round connective tissue cells, large connective tissue monocytes and polymorphonuclear leucocytes, some containing iron pigment granules. Vessels, both blood and lymph, are dilated and newly formed capillaries and proliferative endarteritis are present. Intima proliferations, especially in the subcutis, are accompanied by extravasation of blood. The elastica becomes disorganized in older lesions, especially in the areas of cellular infiltration, finally resulting in reduction of the collagenous tissue and rarefaction of the elastica. With the subsidence of inflammation in older lesions there occurs a deposit of hemosiderotic granules, at first as a fine dust later becoming clumped and taken up by connective tissue chromatophores. Absent are aneurysmal sacculation, telangiectasiae and hyaline degeneration of vessel walls.



Fig. 605.



Fig. 606.

Fig. 605.—Schamberg' disease. (Dr J F Parkins.)
Fig. 606.—Schamberg' disease. (Dr H. J Templeton.)

**Pigmented Purpuric Lichenoid Dermatitis** is insidious in onset, asymptomatic and characterized by tiny red or orange elevated, round papules which become purpuric and which are sepia in color due to the presence of hemosiderin. Symmetric lesions are grouped in plaques upon the legs, thighs lower trunk, rarely on the arms, and never on the chest or head. (Wise and Wolf ADS 31 443, 1935; Michelson and Laymon b. 32 707 1935.)

**Stasis Dermatitis.**—Some cases of varicosity of the leg veins present a network of tiny purplish vessels rather than the usual wide cavernous channels. The skin is likely to be stained with hemosiderin as a result of diapedesis under hydrostatic pressure, which doubles the blood pressure in the ankles over that in the upper part of the

body and especially following trauma or dermatitis of any cause. Proliferative inflammation of the intima of the small arteries occurs in stagnation. The dermatitis appears to be due to extension of inflammation from the underlying vessels to the skin, rather than to chronic passive congestion (Zimmerman ADS 34: 97 1936) Miskjian (ADS 50: 417 1944) stated there is no essential difference between stasis dermatitis and capillaritis, but that the purpuric pigmented angiodermatitis of Favre referring to chronic, deeply infiltrated, purplish brown eruptions on the legs, is not synonymous with stasis dermatitis, which should be diagnosed only in the presence of demonstrable stasis, edema, purple cyanosis and varicosity See Touraine on capillaritis (BSocfrançD 44 837 1937 monographic)

**Angioma Serpiginosum.**—See p. 503.

## VASCULAR GANGRENE OF THE SKIN

Gangrene which may be small or large in quantity can come about only as the result of interruption of nutrition, or toxic or traumatic destruction. Causes of tissue death may be classified

- Intravascular
  - Embolism
  - Thrombosis
- Vessel wall changes
  - Arteritis
    - Trauma
    - Thrombo angiitis
    - Periarteritis
  - Phlebitis
  - Degeneration
    - Arteriosclerosis
    - Acrosclerosis
    - Scleroderma
  - Contraction
    - Raynaud's phenomenon
    - Ergotism
    - Traumatic spasm
  - X-ray radium degeneration
  - Purpuric gangrene
- Extravascular
  - Pressure on vessel
    - Inflammatory effusion
    - Tumors
    - Decubitus
  - Trauma
    - Burn
    - Refrigeration
  - Chemical (mineral acid lye)
  - Factitious
  - Infectious, see p. 18°
  - Allergic
    - Exematous (violent)
    - Drugs (arsenical, iodide quinine)
    - Id tests (tuberculin, Frei)
    - Anaphylactic gangrene
  - Shwartzman phenomenon
  - Trophic defect (syringomyelia, neural leprosy)

**Peripheral Vascular Diseases,** by Allen et al. (Saunders, 1946) is a reference of excellence quoted extensively hereinafter

Emboli and Thrombi, occluding vascular branches, cause infarction of the tissue supplied. The region, often a foot or leg becomes more or less suddenly either ischemic or cyanotic numb and tingling, then painful, later anesthetic. A line of demarcation forms eventually and the dead tissue sloughs. Arterial occlusions may develop suddenly in the presence of severe infectious disease during congestive heart failure postoperatively or in polycythemia vera or other blood dyscrasias. In patients past middle life arteriosclerosis obliterans is the first consideration in differential diagnosis The sudden seizure with severe pain, the absence of arterial pulsation, the cold white extremity with anesthesia and loss of motor power are typical early features, which will be followed by gangrene unless the obstruction proves surgically removable Arterial thrombosis may follow acute or chronic trauma in cases lacking evidence of pre existing arterial disease Penetrating wounds, bruises, and crush injuries are causative.

**Segmentary Arterial Spasm** occasionally results from trauma. Spastic occlusion occurs within 24 hours after the injury and may eventuate in gangrene. A large artery is affected, a distinction from Raynaud's phenomenon, which affect arterioles (Montgomery and Ireland: J 105: 1 41 1933 Cobens Lancet 1:1, 1944)

**White Fingers** is a name that has been used for the vaso-spastic disorder which results *from the use of vibratory tools such as a pneumatic hammer* (Hardgrove and Barker PSMMC 8 343 1933) Characteristically it is not symmetric a difference *from Raynaud disease and it occurs in workmen using vibratory tool in cool surrounding* affecting the left hand of right handed persons. The fingers manifest no pain redness o edema, no persistent sensory changes, no changes in the blood vessels *excepting contracture* and no muscular weakness tremor or cramping. The disorder affects only the fingers starting on the outer half of the index finger and does *not travel* [illegible] *the arm. If it becomes* [illegible] *stablished in the winter it* [illegible] be expected to disappear until warm weather and so it may partially disable the man. Discontinuing the use of the pneumatic hammer did not relieve patients of Gurdjian and Walker (J 129: 668, 1945)

***Symptomatic Gangrene*** may occur in intense localized inflammatory processes. Multiple gangrenous lesions sometimes complicate severe systemic diseases, such as [illegible] phus, typhoid fever malaria, and the xanthemas. See also pyoderma gangrenosum, *treptococcic gangrene, staphylococcic gangrene gangrenous balanitis, dermatitis factitia.* Ulceration of considerable extent may occur in syphilitic gummas, tuberculous and leprous lesions, herpes zoster, smallpox, several varieties of mycotic infection, leishmaniasis, mycosis fungoides, and carcinoma. Trophic disturbances, as seen in [illegible]yringomyelia tabes and other central nervou system lesions, frequently result in gangrene Leprosy [illegible] destroying peripheral nerv[illegible] constitutes [illegible] other possible cause



Fig [illegible] —Arsphenamine dermatitis with [illegible] grene (Rosebe[illegible] ArchD[illegible] 18 [illegible], 1931)

**Toxic Gangrene.**—Peripheral [illegible] gangrene [illegible] to ergotism [illegible] red [illegible] ep lemic f [illegible] [illegible] tilago poisoning [illegible] Ergotam ne tartrate, [illegible] [illegible] the [illegible] of pruritus, [illegible] caused gangrene whe[illegible] given therapeutically

**Anaphylactic Gangrene** [illegible] resulted, [illegible] solated [illegible] from th[illegible] repetition of [illegible] [illegible]

**Decubital Ulcers (Bedsores)** are due to [illegible] cular compres[illegible]ion along with the factor [illegible] debilitation of the victim. The sites of [illegible] redilection over the bony prominences, the sacrum coccyx scapulae elbows, heels, and trochanters. [illegible] prolonged time exceeding 1[illegible] pounds per square inch [illegible] skin will cause necrosis.

Lo[illegible] e [illegible] Pract 138 [illegible] 1937) [illegible] bed types (1) the acute type [illegible] ted with [illegible] of the nervous system unresponsive to treatment and rapidly f[illegible]tal and ( ) the [illegible] type the [illegible] post [illegible] in etiology. Erythema is the early sign. In [illegible] best protection, [illegible] redistribution of weight bearing will prevent further progress. The further [illegible] congestion which does not disappear on pres[illegible] [illegible] useful [illegible] with protective and soothing measures. [illegible] bed at 100 [illegible] pillow under the knees, allowance for curvature [illegible] the [illegible] changes [illegible] gentle massage [illegible] wrinkles in bed [illegible] the [illegible] Irritant [illegible] must not be used [illegible] the stage of [illegible] [illegible] regrowth of tissues. Irritant [illegible] must not be used

Cope (BMJ 1: 73, 1939) stressed the avoidance of long continued pressure and of minor trauma, and advised keeping the skin dry, massage, and elastoplast protection for incipient lesions. Sulfathiazole powder for the ulcers was recommended by Goodman and Cornaro (OhioSMJ 37: 836, 1941). The care of cord injury patients was considered by Munro (NEngJM 223: 391, 1940) who moved patients by an exact hourly time schedule. Bedsores may be excised in some instances and the technic was detailed by Gibbon and Freeman (AnnSurg 124: 1148, 1946).

**Plaster Sores**, occurring beneath casts over bony prominences, usually the tibial tubercle, heel or malleoli, are not fundamentally different from bedsores. Their existence may not be suspected until the odor or sight of the discharge, rather than pain, gives the clue.

**Thrombo-angiitis Obliterans**, according to Allen et al. (Peripheral Vascular Diseases, Saunders, 1946) is a segmental, inflammatory obliterative disease of the arteries and veins which occurs almost exclusively in young men, involves the extremities and rarely the viscera also and produces ischemia of tissues and frequently gangrene. The pathologic picture is characteristic, involving primarily the blood vessels of the extremities and beginning in most cases in the medium sized or small arteries, especially the posterior tibial, anterior tibial, radial and ulnar arteries (the femoral and brachial only in late and severe progressive cases). Arterioles are not affected by the typical pathologic process.

The lesion is an inflammatory, non-suppurative panarteritis or panphlebitis with associated thrombosis but without necrosis of the vessel wall. The thrombus becomes organized by heavy growth of fibroblasts comparatively early and minor recanalization may occur. The lesions are segmental with normal segments situated between diseased segments of the vessels, resulting in occlusion which is permanent and usually complete so that there is destruction or marked impairment of the function of the involved segment of the vessel. Extensive development and enlargement of collateral and anastomotic vessels ensues. Secondary anatomic effects of the disease are the result of malnutrition of tissues, complicated by congestion in some cases and by trauma and secondary infection. Severity is proportional to the rapidity of development and to the extent of arterial occlusions and is inversely proportional to the rapidity and extent to which the collateral arterial anastomoses develop.

Secondary to the vascular lesion, ischemia may produce atrophy of the skeletal muscles, osteoporosis of the foot and leg bones, gangrene, atrophy and resorption of fat, atrophy of skin and distortion of nails, capillary dilation and atony, and ischemic neuritis.

The disease predominantly occurs in young or middle-aged adults, almost exclusively in males, and almost exclusively in Hebrews. Heredity perhaps plays a part. Tobacco has an unarguable harmful effect but a causative relationship is undetermined. Investigations seeking an infectious agent have proved disappointing despite the inflammatory nature of the disease.

Symptoms are due to ischemia, and the outstanding symptom is pain. This is manifest as *intermittent claudication, rest pain, pain of ischemic neuritis*, and pain of ulceration. The inflammatory lesions of the vessels themselves are painful but not severely so. Sensitivity to cold is a frequent and often early manifestation. Paresthesias and muscle weakness occur. One finds marked impairment or absence of pulsation in the posterior tibial and dorsalis pedis arteries in most cases. Color changes include abnormal redness, particularly on dependency. Occasionally there may be cyanosis. Color changes are more significant if unilateral or affecting only certain digits. Raynaud's phenomenon may occur, but its distribution is usually irregular and asymmetrical. Abnormal coldness of the skin may be conspicuous and may affect only certain digits of one extremity. The vascular lesions produce permanent arterial occlusion, and normal function is not restored either spontaneously or as the result of treatment. The lesions are segmental and may be extensive or isolated. Much of the a[illegible]

may be essentially normal. The disease is episodal, characterized by exacerbations and periods of quiescence. In most cases it ultimately becomes inactive, and episodes of new occlusion finally cease. Cases may be clinically divided among (1) the progressive ones, (2) the common, slowly progressive sort, (3) those with sudden occlusion of large vessels, and (4) the relatively uncommon fulminating cases of rapid progression.

Treatment includes attempts to prevent progression of disease, efforts to produce vasodilation, mechanical devices for increasing blood flow, measures to decrease the viscosity and coagulation of the blood, symptomatic palliation of pain, procedures to increase the oxygenation of the ischemic tissues, local treatment of ulcerative and gangrenous lesions, chemicals for combating secondary infection, and finally amputation. Protection of the parts is essential, tobacco must be interdicted, diet is of little help, and bed rest is advised during active phases of the disease with elevation, warmth, and the avoidance of contractures. Hildebrand (BMJ 39: 116, 1943) stated that fever therapy 2 to 3 hour sessions at 103° F., relieves pain in 10 hours and he discussed hygienic care, rest, exercise, baths, heat, sympathetic block, passive vascular exercise, intravenous saline, antispasmodic medication, intermittent venous occlusion, mecholyl iontophoresis, penicillin, ultraviolet light and local surgery.

**Endarteritis and Thrombo-angiitis** resulting in dry gangrene may be syphilitic (rare), thromboarteriosclerotic resulting in senile gangrene, or obliterative. The lesions are usually symmetric and comparatively unresponsive to treatment; they often require surgery.

**Arteriosclerosis**, according to Allen et al. (Peripheral Vascular Diseases, Saunders, 1946) is a broad and loosely used category in which are placed those diseases of the arteries which lead to loss of elasticity, irregular changes in appearance and structure of the medial and intimal coats and ultimately to dilatation, deformity or obstruction of the lumen. These changes are primarily degenerative as distinguished from inflammatory.

Arteriosclerosis obliterans is that type of arteriosclerosis occurring typically in the extremities and eventuating in progressive or episodal occlusion of arterial lumina. It is commonly but not exclusively a disease of the later years of life. It is the most common of peripheral occlusive arterial diseases and accounts for 50 to 60 per cent of such cases. Pathologically one finds in advanced lesions gross enlargement, irregularity and tortuousity of the arteries, with considerably increased consistency and irregular thinning of the medial coat, deposits of calcium which may be in the media or at the base of atheromas, irregular atheromatous formations sometimes projecting considerably into the lumen and partial or complete occlusion of the lumen by gray or red thrombi. The 3 essential components of the lesion are atheroma, thrombosis and destructive degeneration of the medial coat. The relative proportions of these components vary considerably in various cases.

In thrombo-angiitis obliterans the pathologic changes include marked fibroblastic proliferation, late periarterial fibrosis, marked endothelial proliferation of the vasa vasorum in the adventitial coat, good preservation of the medial muscle without calcium deposits, and diffuse fibroblastic proliferation especially about vasa vasorum; the intima shows no atheroma, lipoid or calcium, but proliferation of the endothelium is marked; and the thrombus is extremely cellular in its organization.

Ischemia produced by arterial obstruction from arteriosclerosis obliterans may be augmented by arteriolar constriction from any cause such as exposure to cold or the use of tobacco. It may be lessened by vasodilation produced by heat or by various vasodilating therapeutic procedures. The arterioles in extremities affected by arteriosclerosis obliterans are however in a condition of normal tone most of the time and are susceptible either to vasodilation or vasoconstriction. If the degree of arterial ordi-

sion is not too extensive considerable improvement of the circulation may be possible as the result of arteriolar dilation. Obstruction of a large artery produces lowering of arterial pressure in the smaller vessels distal to the point of obstruction and the slowing of blood flow

Symptoms result from ischemia of tissues and are mostly confined to the lower extremities. The symptoms may progress in a series of episodes with partial regression between episodes. Such symptoms include the following

Intermittent Claudication a symptom and not a disease indicating inadequate supply of arterial blood to contracting muscles. It never occurs in the legs as a result of standing, reclining or sitting, and has no relationship to muscle cramps which patients have in bed. It is brought on only by continuous exercise and is relieved promptly by discontinuance of exercise without change of position of the affected parts. It is usually unilateral at first, becoming bilateral, and continues to be worse in one leg than the other. It may exist for years as the only subjective manifestation of the disease. The distance that the patient is able to walk before the distress of intermittent claudication develops varies with the extent of arterial occlusion and the level at which this has taken place.

Rest Pain resulting from severe ischemia and advanced disease. It is usually felt first in the digits but may involve the foot and leg as well. It is noted at night commonly consisting of dull to moderate aching pain which interferes with sleep. It develops after acute arterial occlusion or may result from gradually increasing arterial occlusion.

Pain of Ulceration and Gangrene, provoking usually moderate t severe pain. Some patients do not suffer much, although opiates are required for others, some of whom can scarcely be relieved. It persists over long periods of time and is worse at night. It is usually confined to the region f ulceration or gangrene or just proximal to it.

Pain of Ischemic Neuritis, occurring over large portions of the skin and perhaps involving the distribution of the peripheral nerve trunks. It occurs in the absence of ulceration, but if this is present it extends proximally from the regions of ulceration for a considerable distance. It may be steady or paroxysmal, and sometimes there are lightning pains. It frequently severe and difficult to relieve. It occurs more commonly among diabetic than nondiabetic patients.

Other Sensory Disturbances, including paresthesias, numbness and burning. Cold sensitivity is a complaint in some patients early in the disease. Muscular weakness is associated with a considerable degree of arterial insufficiency and stiffness of joints gradually develops in association with disuse and muscle weakness.

Physical findings include impaired arterial pulsation color changes with redness of the feet or bluish discoloration in severe cases, sometimes marked pallor of one or more toes postural changes of color with abnormal pallor on elevation and rubor on dependency with delay in return of color and of filling of veins on dependency and temperature changes due to inadequate blood supply. Ulceration, gangrene, and infection may develop

Spontaneous ulceration or gangrene usually develops first in the terminal portions of the digits, often around the nails. Either may develop as a result of the pressure of shoes in ordinary walking. Ulceration of the foot or leg is usually the result of mechanical or thermal trauma or pyogenic infection. Sometimes it develops in eczematoid lesions. When ulceration and gangrene occur in arteriosclerosis obliterans, they are usually of the dry type and accompanied by little or no systemic reaction. When diabetes is present the lesions are more likely to be moist and there may be considerable systemati reaction with the rapid development of lymphangitis and even septicemia. Roentgenograms of the legs may visualize calcification of the arteries or osteoporosis. Diabetes mellitus is often present

detectable by the carbohydrate tolerance test. Plasma lipoids are frequently elevated and lipemia and xanthoma are common concomitants of arteriosclerotic disease.

Differentiation of thromboangiitis obliterans from arteriosclerosis in patients between 40 and 50 years of age was clarified by Silbert (J 129 5, 1945) whose patients with thromboangiitis abstained from smoking for 10 years and remained arrested during that time. the patient with thromboangiitis appears younger than his age (the arteriosclerotic older) his hair is normally pigmented rather than gray the arcus senilis is absent; the retinal arteries normal the blood pressure low; the radial and temporal vessels soft the upper extremities possibly involved the femoral arteries perhaps occluded; the vessels not calcified the blood volume diminished; the coronary artery not sclerosed the aorta normal on x ray examination; albuminuria infrequent and a history of migratory phlebitis frequent.

Spasm is differentiated from occlusion by the thermal reflex vasodilation test (Saland et al. AmHJ 17: 551 1939) which is accomplished by immersing the hands and forearms in water at 43 C. and recording the temperature of the great toe a rise in which should begin normally within 13 minutes, reaching 30.5 In no case of obliterative arteriosclerosis, among his 73 patients so studied did it do so.

DIFFERENTIATION OF ARTERIOSCLEROSIS OBLITERANS AND THROMBO-ANGIITIS OBLITERANS

(Allen et al Peripheral Vascular Diseases Saunders 1946)

| DISTINGUISHING FEATURES | THROMBO-ANGIITIS OBLITERANS | ARTERIOSCLEROSIS OBLITERANS |
|---|---|---|
| Age at onset of symptoms | Almost always under [illegible] | Almost always over [illegible] |
| Sex | Males [illegible] per cent | Males [illegible] per cent |
| Involvement of upper extremities | [illegible] per cent of cases | Rare |
| Presence or history of superficial thrombophlebitis | [illegible] per cent of cases | Never |
| Roentgenographic calcification of arteries | Absent | Present in [illegible] per cent of males |
| Hypertension | Rare in early years of disease | Present in 31 per cent of cases |
| Diabetes mellitus | Rare in early years of disease | Present in 20 per cent of cases |
| Plasma lipoids | Usually normal | Frequently elevated especially in younger patients |

TREATMENT OF ARTERIOSCLEROSIS OBLITERANS involves, according to Allen et al (Peripheral Vascular Diseases, Saunders, 1946) these general considerations (1) the disease is organic and no treatment is yet known which will open the lumen of an artery occluded by the sclerotic and thrombotic process (2) the disease is common among old people whose capacity for healing would be poor even if ischemia were not present (3) the disease tends to be progressive once it has become manifest (4) the disease is more widespread than apparent on clinical examination and (5) it is often associated with aged persons nonvascular diseases which will terminate their lives. The basic principles of treatment include a protective regimen for the conservation of tissues of impaired blood supply and measures to promote vasodilation to prevent vasoconstriction to relieve pain symptomatically to encourage ulcers to heal to limit the progress of gangrene and to control lipemia and diabetes and so perhaps to prevent progression of the disease Amputation is the resort when other treatment fails

The care of the feet is fundamental and requires that the patient be given detailed instruction to avoid mechanical chemical, or thermal injuries. The feet must be clean and carefully dried after bathing Toenails should be cut carefully and with the avoidance of injury to the skin Corns and calluses should not be cut except by an expert who is aware of the hazards. Shoes must be carefully selected. Exposure t

cold is to be avoided. Tinea of the feet requires nonirritating attack. The di be comparatively low in calories and in fat, for lipemia and obesity must be and diabetes mellitus requires control if it is present. Tobacco should be int Alcohol in moderation may be permitted. Coffee and tea do not require res Exercise should be limited to the capacity of the patient avoiding intermittent c tion. Occupational hazards require consideration. The climate should be com and warm.

Details of medicinal and physical therapeutic measures and the surgical aspe obliterative vascular disease are omitted from consideration here. The article o Kittrick (J 113: 1223, 1939) is commendable. Treatment of all hospitalized pa includes be noted, bed rest careful hygiene, general support ve measures. Buer postural exercises and intermittent venous hyperemia. By careful attention to de and by learning to live within the circulatory possibilities of their feet, many pati in the earlier stages of obliterative disease may avoid or at least postpone the onse gangrene for many years by simple methods, but there are unsuccessful in more vanced cases. Intravenous calcium proved harmless and yielded a feeling of warm along with appreciable increase in pulse amplitude and relief of night cramps and r pain in patients of Weichsel (AmIntM 13 1150, 1940). Calcium must not be given digitalized patient. While mechanical blockage of vessels is of primary significanc some of the symptoms and signs are due to spasm, and interruption of vasoconstricto impulses by procaine infiltration of sympathetic ganglia relieves these. Ochsner an DeBakey (J 114: 117 1940) reported much benefit in thrombophlebitis so treated DeTakats et al. (J 131: 495 1946) recommended sympathectomy if the temporary block gave good results, in arteriosclerosis. The oscillating Sanders bed relieves pre trophic pain and the pain of ischemia, ulceration, and gangrene according to Barker and Roth (AmHJ 18: 312 1939).

**Diabetic Gangrene** occurs in patients suffering from diabetes mellitus, slight injuries of the skin predisposing to the development of it. The lesions are rounded oval, or irregular in outline, and may be so deep as to involve osseous as well as cu taneous tissue. The onset may be gradual or sudden. The lesion may be more or less symmetrical, and the formation of the gangrenous patches may be preceded by the development of bullae. Toes are especially vulnerable and gangrene may be initiated by minor surgical procedures such as the treatment of an ingrown nail or a corn. Gangrene is the local manifestation of a systemic disease and mortality depends on the extent, duration, systemic febrile reaction before the onset of gangrene recurrence infection and, most of all, the preoperative and postoperative measures employed. Wounds in diabetics heal as well as they do in nondiabetics (Greene et al. J 115 1518, 1940).

Of a ... cases of gangrene associated with diabetes reviewed by McKittrick (ASurg 40 ... 332, 1940) the sex distribution was about equal the average age was 64 the aver age duration of diabetes prior to the development of gangrene was 8.7 years, the over all mortality was 9.4 per cent and mortality after major amputations was 14 per cent Guides to the appropriate surgical management were set forth by Williams and O'Kane (ASurg 40 643 1940) in accord with the classification of the lesions as purely vascula purely infectious, or intergradients mixed in various degrees. The majority of purely vascular superficial lesions do well without operation. If infection can be controlled. Lo calized noninfected vascular lesions ... do not occur calf or thigh amputation must be selected depending on the results of examination of the circulation of the limb. Marked vascular impairment together with prevailing infection in the ... usually unavoidable. The better the ... the more localized ... be the efforts to deal with infection.

Prognosis is unfavorable but less so than before treatment with insulin was in stituted. Gangrene however generally requires amputation. Horton (J 111 ... 194, 1939) reported that with recent methods of management the expectation is that some 42 per cent must undergo amputation and that 70 per cent can get along for 3 years after the onset of symptoms without requiring surgical intervention, 60 per cent for 5 years, and 40 per cent actually for 10 years.

Proper care of the feet prevents complications in diabetes. Cleanliness, correc tion of defects, immediate attention to minor derangements, treatment of tinea if it is present, prevention of constriction, and ... are needful. Crossing the legs is unwise. Liberal diet and control of glycosuria are valuable preventive measures.

**Raynaud's Phenomenon** may be defined as episodes of constriction of the small arteries or arterioles of the extremities resulting in inter

## DIFFERENTIAL DIAGNOSIS OF RAYNAUD'S DISEASE, ACROCYANOSIS, LIVEDO RETICULARIS, PERNIO AND ACROSCLERODERMA (ACROSCLEROSIS)

(Allen et al. Peripheral Vascular Diseases, Saunders, 1946)

| | RAYNAUD DISEASE | ACROCYANOSIS | LIVEDO RETICULARIS | PERNIO | ACROSCLEROSIS |
|---|---|---|---|---|---|
| Sex and age | Girls or young women in 70 per cent of cases | Girls or young women in 90 per cent of cases | Women or men of any age | Young women in 70 per cent of cases | Young women in 85 per cent of cases |
| Type of color change | Blue, red, white mottled or diffuse | Blue, diffuse | Red, blue mottled and reticulated | Blue, red, localized | Blue, red, white mottled or diffuse |
| Location of vascular symptoms | Fingers, toes. Nose and ears rarely | Hands usually Feet occasionally | Legs usually arms occasionally | Exposed surfaces, legs especially | Hands and feet |
| Duration of vascular symptoms | Intermittent | Permanent | Permanent | Variable worse in winter | Intermittent |
| Local symptoms | None or burning pain | Usually none | None or coldness and pain | Marked itching and burning | Stiffening and tension of skin |
| Effect of cold | Symptoms increase | Symptoms increase | Increase of blueness | Causal increase of redness | Symptoms increase |
| Effect of heat and vasodilatation | May decrease color changes greatly | Little change | Less blueness | More redness | May decrease color changes |
| Effect of posture and exercise | Little change | Cyanosis decreases on elevation | Cyanosis decreases on elevation or exercise | No change | No change |
| Swelling | Slight or none | Slight or none | Slight or none | Slight or none | Slight to moderate |
| Necrosis and ulceration | Slight or limited or none | None | Occasionally in severe cases | Always in severe cases | Frequently in association with marked scleroderma |



Fig. 408.—Gangrene in diabetes.



Fig. 409.—Gangrene in diabetes.



Fig. 410.—Diabetic gangrene.

mittent changes in color of the extremities, such as pallor cyanosis, or both (Allen et al. Peripheral Vascular Diseases, Saunders, 1946). It occurs not only in Raynaud's disease but also secondarily. It denotes functional changes in the peripheral circulation. Conditions with which it may be associated include

Traumatic
    Occupational—pneumatic hammer disease
        vasospasm of typists pianists
    Following injury or surgery—
        associated with Sudeck's atrophy
        arteriospasm
Neurogenic Lesions
    Cervical rib and scalenus anticus syndrome
    Diseases of the nervous system
Occlusive arterial disease
    Arteriosclerosis obliterans
    Thrombo-angiitis obliterans
    Embolism
Intoxication with heavy metals or ergot
Miscellaneous diseases, including scleroderma and lupus erythematosus



Fig. 611.—Raynaud's syndrome with digital gangrene. (Dr Grover Wende.)

**Raynaud's Syndrome** is characterized by paroxysmal attacks of vascular spasm of unknown etiology which cause ischemia (10 per cent of the cases) or cyanosis (90 per cent) of the parts involved. Pallor is due to arteriolar spasm such that blood does not enter the capillaries; cyanosis when present is due to stagnation in widely dilated capillaries. It attacks females in 5:1 preference to males, and almost ⅘ of the cases begin before age 40. Heredity, psychosomatic makeup and perhaps the endocrine balance of the patient are etiologic factors. Fingers and toes, less often nose or ears, are affected. The hands being warm, cooling of the body may nevertheless cause an attack, and warming of the body will relieve an attack, although it will not if the hands are exposed to cold. Since attacks can be produced by cooling the fingers after preganglionic sympathectomy, attacks must be due to a local vascular fault, argued Lewis (ClinSc 3: 321, 1938), but Simpson et al. (PSMDC 5: 29, 1930) are among those who

judge the fault to lie primarily in the vasomotor system. Severe throbbing pain, or anesthesia may be followed by necrosis. Recurrence in an amputation stump is common.

The relationship of Raynaud's phenomenon, sclerodactylia, and scleroderma was clarified by Brown et al. (AnnIntMed 6: 531, 1930) who found that acrosclerosis (q.v.) associated with attacks of digital ischemia is responsive to sympathectomy, but advanced cases are characterized by such vascular destruction that irreparable damage having already been done, sympathectomy is futile. Benefit may be obtained from vasodilation with Mecholyl, a vasodilator by parasympathetic stimulation. *Histamine iontophoresis and intravenous papaverine produce increased volume of the capillary bed and* promote healing of trophic lesions, reported Mulinos et al. (AmJMSc 19: 793, 1939).

The name "Raynaud's Disease" should be limited in connotation, according to Allen et al. (1946), the typical case being that of a young woman who first observed color changes of the Raynaud's phenomenon type on exposure to cold. Usually the onset of such color changes is gradual, although in some instances they may be called dramatically to attention by an acute episode of pallor in one or two fingers on exposure to cold, the "dead finger" phenomenon. In the early stage of the disease only the tips of all fingers of both hands are involved. Later the changes in color of the skin involve more of the proximal parts of the fingers until in the late stages the color changes may extend back to involve the hand. Symptoms are worse in the cold season and better in the warm season. Pain is not a prominent symptom during the attack or in the *interval between attacks. Paresthesia occurs commonly during the attack* and consists of numbness, tingling, burning, a feeling of tightness, "pins and needles" sensation or sticking in the fingers. During the attack the fingers are cold, and sensory acuity may be diminished. Slight swelling may occur and may persist even during interval between attacks. In the progressive or advanced stages of Raynaud's disease Raynaud's phenomenon may become disabling in its severity and *frequency*. The attacks may follow exposure to a slightly cool environment and almost any emotional stress. Sclerodermatous changes of considerable degree may affect the involved parts and interfere with normal use of the extremity. Although extensive gangrene does not occur, the gangrenous ulceration of the tips of the digits may be persistent and may cause considerable discomfort.

**DIFFERENTIAL DIAGNOSIS OF RAYNAUD'S DISEASE, THROMBO-ANGIITIS OBLITERANS, AND ARTERIOSCLEROSIS OBLITERANS**

(Allen et al.: Peripheral Vascular Diseases, Saunders, 1946)

| | RAYNAUD'S DISEASE | THROMBO-ANGIITIS OBLITERANS | ARTERIOSCLEROSIS OBLITERANS |
|---|---|---|---|
| Sex | Females in 90 per cent of cases | Males in 99 per cent of cases | Males in 85 per cent of cases |
| Age of onset (years) | 12 to 30 | 20 to 40 | Over 50 |
| Color changes, Raynaud phenomenon | 100 per cent of cases | 30 per cent of cases | 10 per cent of cases |
| Postural color changes | Absent | Frequently present | Frequently present |
| Gangrene (if present) | *Limited to small areas of skin* | *Minimal to* extensive | Minimal to extensive |
| Involvement of upper extremities | Almost all cases | 40 per cent of cases | Rare |
| Involvement of lower extremities | Usual but less frequently than of upper extremities | 98 per cent of cases | 100 per cent of cases |
| Symmetry | Bilateral and symmetric | Asymmetric but usually bilateral | Asymmetric but usually bilateral |
| Peripheral arterial pulsation | Present | Impaired or absent | Impaired or absent |
| Calcification of arteries | Absent | Usually absent | Usually absent |
| Superficial phlebitis | Absent | 40 per cent of cases | Absent |
| Acrosclerosis | Sometimes present | Absent | Absent |

# DERMATOSES OF NEUROLOGIC AND PSYCHIATRIC ORIGIN

## ABNORMALITY OF SENSATION

**Causalgia** is a neuralgia featuring burning pain of a sort that i tolerable until the patient is touched becoming far worse if the patient, who dreads t, is touched. It is due perhaps to nerve ischemia (see under glossy skin) and occurred in a case of arterial embolism described by Homans (NEngJM 222 870 1940) It usually results from peripheral nerve injury and is associated with trophic and secretory phenomena. When the brachial plexus is affected, the fingers are usually tapering, smooth, hair less, almost devoid f wrinkles glossy pink, ruddy or blotched as if with permanent chilblains, nd the intensity of suffering varies from th most trivial burning t a state of torture which can hardly be credited but reacts on the whole economy until the general health is seriously affected. Exposure to the air is avoided by the patient with a care which seems absurd, and most f the bad cases keep the hand constantly wet. The patient walks carefully carries the limb tenderly with the sound hand, is tremulous, nervous and has all expedients for lessening his pain, quoted by Spengel and Milowski (J 127: 9 1945) The symptoms can develop w thout blood vessel damage The sensory deficit does not necessarily outline the area of causalgia. Percussion of the involved nerve at the site f injury caused tingling in its distribution but no change in the pain. Diffuse decalcification of the extremity develops, and immobilization by the patient may even result in pressure sores. Sympathectomy may relieve pain but it must be complete and should not be performed unless preliminary procaine block indicates its probability of success (Ulmer and Mayfield BGO 83 789 1946) The pain path is in Lewis' ... system, and pain originates peripherally it may per sist or return after chord tom or after section f posterior roots depending o which severs the main pathway via the sympathetic ... to th ... cord ... or via the posterior root of the injured nerve (Bingham BMJ 2 334 1945)

**Dermatalgia** is pain in the skin ot consequent to any ppreciable structural lesion. The disorder is usually secondary t hysteria or some rganic disturbance of the nerve centers, especially the cord. Localized areas, particularly on the hairy parts, are affected. It frequent in tabes, and is occasionally met in diabetes mellitus.

**Erythromelalgia** is a disorder of the extrem ties characterized by hooting, throbbing, or burning, neuralgic pains, accompanied by congestion and patchy redness f the affected parts. The affection may be unilateral or bilateral and one or both hands and feet or all fou extremities may be attacked There may develop atrophic changes in the invol ed parts. The patient may be man woman, rarely a child for symptoms usually become manifest in middle age or later

Characteristic features include (1) attacks of burning pain, symmetric in the hands or feet ( ) aggravation by dependent posture, exertion or heat; (3) rel ef by elevation or cold (4) flushing, congestion and warmth of the skin during the attack; and (5) refractoriness to treatment (Brown AmJMSc 183 468, 1932) Exacerbations sometimes last for hours, again for only few minutes. Allen and N rman (USNMBull 35 309 1937) divided the cases into those which are primary and those which are secondary to peripheral neuritis, polycythemia, or thallium poisoning. Some swelling and puffiness may be present i the localized burning region, or the whole ex tremity may be slightly swollen N evidence of occlusive arterial disease is found in the idiopathic type In treatment modest doses f aspirin may yield relief.

Symptoms are allayed by the avoidance of anything which produces vasodilation f the extrem ties Hyposensitization to warmth by immersion f the part in water the temperature of which is increased progressively with subsequent treatment, may prove helpful, but this approach is not dependable. X ray therapy may help. Sympathectomy was reported curative in 3 instances (Telford and Simmons BMJ 2 782, 1940) Erythermalgia is the name preferred by Smith nd Allen (PROMC 14: 236 1939) who distinguished the burni g paresthesia of the occlusive vascular patient by the lack in such cases f temperature elev tion f the affected extremities.

**Hyperesthesia** is a functional disorder characterized by exaggerated sensiti eness f the ffected part The condition is symptomatic The distribut on may be uni ersal but is generally localized It may be unilateral or bilateral and trans ent or persistent the duration depending on the underlying cause Hyperesthesia may be due t inflammation of a viscus of the same segment l innervation as that area f the skin in which the symptom ppears, as in ppendic tis or salpingitis. Hyperesthesia may be caused by excess f caffeine f tigue and anxiety It occurs as a symptom in i fluenza, dengue,

tabes dorsalis, the pink disease ischemic neuritis peripheral vascular diseases, trigeminal neuralgia, and neuritis following herpes zoster. Burning of the soles was noted in experimentally induced vitamin $B_1$ deficiency by Jolliffe et al. (AmJMSc 193: 193, 1939)

**Hypoesthesia.** Loss of sensibility of the skin occurs in hysteria, neuritis, lepra, and neural disorders such as spinal cord lesions and occlusive peripheral vascular disease. A pincushion man was interestingly described by Critchley (BMJ 891, 1934). Such individuals undergo severe injuries without giving evidence of experiencing pain. (Ford and Wilkins: BullJHH 62: 448 1938.)

**Itchy Points in the Skin** is a rare disorder which has been confused with neurotic excoriation. No objective indication of abnormality exists unless this be excoriations. Itching is sharply localized to one or a few pinhead size sites, always discrete usually overlying a bony prominence. The nature and cause of the disease are unknown (Toomey: ADS 5 44 1922). One might remove the skin at the specified spot by means of a cutaneous punch.

**Meralgia Paresthetica** affects only the external femoral cutaneous nerve, which supplies the outer side of the lower two-thirds of the thigh. It is characterized by hyperesthesia or anesthesia, and sensations of pain numbness and formication. Severance of the nerve is therapeutically effective (Lee: InternatClin 1 *10, 1936.)

**Paresthesia** is abnormal sensation, such as burning prickling, numbness, or formication. It is of neuropsychiatric import the dermatologist rarely being competent to interpret its significance. It occurs in occlusive peripheral vascular diseases. A type of unknown cause is characterized by widely disseminated discrete areas where itching, tingling, and crawling sensations are experienced and the patient is led to believe himself or more often herself to be infested with parasites. Many cases of this sort are labeled acarophobias (q. v.) It is usual for these cases to be obscured by dermatitis venenata due to medicinally applied irritants. Large doses of vitamin A may relieve an underlying lichen spinulosus.

**Segmental Neuralgia,** with hyperesthesia and often tenderness tingling, sticking and burning sensations, limited to sharply defined areas, is a fairly common occurrence. It is probably an abortive form of herpes zoster (Davis J 10? 1620 1936). It is often responsive to therapeutic intracutaneous injection of vaccinia virus.

**Syringomyelia** is a disease of the spinal cord manifested by sensory and trophic changes, particularly in neural tissues of the upper extremities. The patient shows slowly developing sensory loss followed by motor defection usually beginning in one upper extremity. Diagnosis is not stereotyped, but dissociated sensory loss in the arms muscular atrophy of the hand, and painless burns are practically pathognomonic. Failure to experience pain results in the patient's unwittingly injuring himself, and the cutaneous lesions are blisters and ulcers, which are painless. Changes are found in the cord, and consist of cavities in the posterior horn. The cysts are thought to be degenerated gliomas, representative of a mesodermal defect in dorsal closure of the embryonic neural tube.

Syringobulbia is the name applied when the medulla is involved. The trophic ulcers of face and neck resulting from this were described by Schwartz (ADS 41: 153, 1940).

The distal phalanges are often over long and a relationship with arachnodactylia (Marfan syndrome Barro NCarolMJ 3 333 194 ) has been postulated. Facial asymmetry a thin face with chin sharp and nose off center is usual. The malady may bear striking clinical resemblance to neural leprosy other manifestation which can be found if present. The disease is incurable the treatment simply palliative. Tonics and ... may be employed. The cutaneous lesions are to be treated symptomatically care being taken to guard the affected parts from trauma and extremes of temperature. Surgical attack, with laminectomy vertical cordotomy and drainage of the fluid from the cavities, has been undertaken with improvement in some cases. Putnam (MCNAm 10 15 1 1930) preferred x ray treatment of the cord early in the disease.

## TROPHIC LESIONS AND PERFORATING ULCER

**Trophic Changes** occur especially in tissues which have been deprived of pain and temperature sensibility (Karnosh and Scherb J 115 2144 1940). Persistent erythematous lesions sometimes follow section of the fifth nerve and are limited to its distribution. Destructive lesions of the brain stem produce trophic disorders. Sores around the nasal alae especially just inside the nostril sometimes on the cheek or forehead, occasionally occur after gasserian injections (Harris Brain 63 209

1940) Similar ulcers have been noted in lethargic encephalitis (Rosenberg and Solovay ADS 39 829 1939) The individual with a sensory loss is likely to finger and pick at the area more or less unconsciously producing lesions which are basically artefacts but which are likely to be interpreted as trophic in origin.

**Perforating Ulcer** is a type of chronic ulcer of the extremities characterized by the development of a deep sinus at some pressure area, in association with neural or vascular abnormality The affection is an occasional complication of central nervous system syphilis, spina bifida, leprosy and occlusive peripheral vascular disease The earliest lesion is a callus or a ruptured blister near the base of the first phalanx of the great toe, or on the heel. Suppuration takes place and the center sloughs, leaving a superficial circumscribed ulcer surrounded by a thick, horny collar Tenderness is wanting Sinus formation may proceed slowly or rapidly The lesions are usually single but they may be multiple The course is slow but progressive, and even if improvement occurs it is commonly only temporary



Fig. 412.



Fig. 413

Fig. 412.—Syringomyelia, with trophic lesions
Fig. 413.—Perforating ulcer in tabes dorsalis

The condition can be ameliorated by absolute rest of the part but the lesions generally recur when the patient begins to use the limb again. Aside from the treatment of the parent disorder the management is conservative and symptomatic amputation is a last resort (Tocantins and Reimann J 112 2251 1939)

## PSYCHOSOMATIC ASPECTS OF DERMATOLOGY

The transition from conventional and old fashioned thinking about the nature of disease is in an active state of flux, such that the word psychosomatic itself grates upon the sensibilities of many an expert in psychiatry

competence in whose province we do not claim. But materialism is wholly unsatisfactory as we ourselves have pointed out in lay lectures, utilizing such arguments as this: you can have a leg cut off and still be you, and another leg and a couple of arms, and ears, and the appendix removed, and the tonsils yet all the while you have not been touched as these things were being done to something that is yours so by extrapolation, the body may be completely removed and the self persists, and the self (ego) is a more significant thing than the body The mind conscious, feeling or unconscious, takes precedence over the most patently material objective, man-made thing for the very building in which you sit made of bricks and cement and steel girders, existed in the desires and imagination of a mind and was drawn on paper before it was constructed In considering an individual who is ill one is rightly importuned nowadays to turn from the local manifestations to contemplation of the pathology of the person (Wright Clin 3 711 1944) and in dermatology to reflect upon the skin as an organ of expression

As the inflammatory reaction involves dolor calor rubor and tumor so the psychoneurotic reaction involves dolor pallor sudor and tremor *The sufferer from emotional tension may exhibit stomach trouble and may* attribute his woes to this, as every practitioner knows and the sufferer from psychosomatic difficulties may manifest cool sweaty extremities and pompholyx which is prone to become secondarily infected and may prove incurable by materialistic medical means, while his disease can be attacked by psychiatric measures.

If this approach is elementary it embodies the thinking whereby we ourselves are gradually being converted toward views expressed by Stokes et al (AmJMSc 198 577 1939 200 560 1940) Obermayer (J 122 862 1943) and Becker and Obermayer (Modern Dermatology Lippincott 1946) The last provide an essay under their discussion of neurodermatitis, on the mechanism and correction of functional dermatoses, which must be read by those interested. In brief they explain to the patient his nervous irritability and exhaustion, of which he is more or less unaware until they point it out they endeavor to reassure to hold confidence to save the patient's face by attributing his nerves to his inheritance and to teach him to relax by diminishing his ambition by inducing him to take vacations, and by putting him prone daily under a sunlamp and in afternoon naps and they give him mild sedation with phenobarbital if this appears justifiable How much of their thesis deserves universal acceptance it is not possible for us to say for through the peculiarities of our own makeup, we are skeptical But we have seen Becker cure a patient after 6 weeks of hospitalization whom we failed to cure as an outpatient and we desire to give credit where credit is due See pp 36 and 37

The mechanisms of adjustment were interestingly defined by Menninger (JKansMS 44 325 1943) who listed compensation sublimation rationalization symbolization introspection identification condensation, idealization, repression displacement phantasy ambivalence projection, and dissociation The terms are technical ones. If one comprehends them, one may find clues to the reasons for existence of dermatoses which have psychiatric relationships

The relations of the psyche soma, and skin have been discussed by many and we quote as typical the article of Cormia (ADS 55 601 1947) As the eye is the mirror of the soul, so may the skin reflect the psychosomatic personality and its struggles with life. Conflict and tension are produced and they may be partially relieved by the de-

velopment of somatic symptoms. These symptoms are an expression of and a defense against conflict. Weiss and English (Psychosomatic Medicine, Saunders, 1943) speak of "organ language" by which a mute repressed patient expresses himself. A patient with neurotic vomiting is trying to relieve himself of a personally nauseating or intolerable situation one with hysterical blindness is shutting out unwelcome sights. The symbolism of symptoms is nowhere better shown than in the skin. It is expressed both in the type and in the localization of the dermatosis. The skin has the power of expressing many bodily emotions, including those of worry (picking) anxiety (pruritus and sweating) fear and anger (urticaria) guilt and shame (blushing and rosacea) hostility masochism and eroticism (dermatitis factitia) and sexual pleasure (cutaneous masturbation) A patient with urticaria may be bursting the bonds of restraint pruritus and excoriation may represent a martyrlike expression of a desire to scratch a disagreeable environment; while severe dyshidrosis may reveal an unconscious protest against using the hands for an irksome or fearful duty Similarly a patient with rosacea is branded with the permanent guilty flush of self-consciousness and social anxiety A victim of factitial dermatitis openly expresses his hate social resentment and antisocial (destructive) tendencies and at the same time exhibits in obvious fashion his demand for attention and sympathy (narcissism, or self love) A person also attempts, by the localization of his dermatosis, to point out the portion of his environment with which he is coming in conflict and at the same time to make even more clear the essential nature of the conflict A patient with generalized pruritus is resentful against his entire environment pruritus involving the genital region may be due to a sexual conflict; and pruritus ani may be symbolic of a latent homosexual tendency Alopecia areata of the scalp is symbolic of a hole in the head and as such may express inadequacy Case histories exemplifying such conceptions are given by Cormia, and are typical psychoanalytic reports in that they convey conviction to some and provoke in others a desire to explain the dermatoses in some other way which seems more likely to be true

Attention may be called to another one among the profusion of psychologic studies, this by Wittkower and MacKenna (BJD 59 281 1947) indicating that subjects of seborrheic dermatitis are more likely to be grossly inhibited in social contacts conscientious, worrisome anxious, and unable to relax, than members of a control group. The authors aim at unbiased expression and the conclusions are adequately hedged.

Self-inflicted lesions are conspicuously psychoneurotic in etiology while other lesions are explained in a manner borderline dubious, or to ourselves, incredible We incline to think that many an observer sees from within outward in his mind reading and the distinction of fact from fancy is extremely difficult It is our experience time after time, to cure pruritus by the exclusion of a contact irritant after the patient has received a diagnosis of nervous imbalance from another physician. What the psychiatric approach undeniably may accomplish is respite from medication, much of which is irritating, so that the skin heals since it is let alone (Sutton JMoSMA 44 481 1947) If feelings influence the thoughts of those who discuss these problems in these ways, it is safe to say that the psychiatrically inclined are as intensely so influenced as those who profess to keep their feet on the ground, and who in moments of levity compare published psychoanalyses of patients with obscure dermatoses to the interpretations put upon cranial bumps by the phrenologists of a generation ago We wish we knew how psychosomatic dermatology will read in the year 2048.

## NEUROTIC EXCORIATIONS AND DERMATITIS FACTITIA

**Self Inflicted Lesions** were classed by Stokes and Garner (J 93 438 1929) as neurotic excoriations of the skin probably including habit tics hysteric dermatoses and malingering with intent to deceive

**Neurotic Dermatitis and Excoriation.**—Deception is not the essential feature. These cases may be included within 4 types (1) neurotic excoriations or dug-out lesions (2) acne urticata (3) excoriated acne (q v )



Figs. 614 and 615.—Neurotic excoriation in an aged, half blind, despondent patient.



Fig. 616.



Fig. 617.

Fig. 616.—Neurotic excoriation. (Dr. George M. MacKee.)
Fig. 617.—*Dermatitis factitia.* (Dr. Sam Sweitzer.)

and (4) self inflicted lesions made without intent to malinger (auto-lesionism) Women are more often affected than men. The excoriations may occur on any part of the body but the face, lateral aspects of the extremities and the shoulder regions accessible to the finger tips are the sites of predilection. Lesions are produced by picking digging or scratching, which may be quite unintentional and may constitute a more or less unconscious habit analogous to nail biting Emotional and nervous states in masochism and other sex complexes may lie in the background of neurogenous dermatitis. Psychiatrists sometimes go too far with the specious argument that because scratching is pleasurable itching is a result of libido A sound personality may itch, scratch, and be comforted but neurotic excoriation is rationalized by not induced by itching It often indicates sexual tension, sometimes immense boredom Lichen spinulosus, responsive to massive doses of vitamin A (Garfield ADS 45 423 1942) sometimes is responsible for the inconspicuous lesions that tempt the finger tips. Some of these patients need thyroid and improve when it is given (Goldblatt and Gordon JMed 21: 480 1941) Extreme and interesting examples were noted by Senear and Shellow (ADS 46 824, 1942) Psychiatric motivation was discussed by Michelson (ADS 51 245 1945) who stressed the necessity for studying the personality of the patient and recognized the dermatologist s incompetence in the specialty of psychotherapy

In the feeble-minded, bites are common self inflicted lesions (Butterworth and Wilson ADS 38 206, 1938) Biting sucking and similar oral preoccupations may produce circumscribed calluses resembling warts, keloids, or even neoplasms (Ronchese J 127 1050 1945)

**Trichotillomania** is characterized by an abnormal desire of an apparently sane person to extract his own hairs. Children often do this, sometimes eat the hair they pull out. Raymond's designation, *tic de l'épilation* is an appropriate one. The scalp, eyebrows, and lashes are the parts most frequently attacked. One must distinguish alopecia areata and tinea capitis. The application of various antipruritics, such phenol, menthol, camphor or tar, has no effect on the course f the disease. G tta percha can be used as an impervious dressing Trichotillomania can generally be cured by keeping the scalp shaved for several months. Effort should be made to reduce the emotional tension of the affected youngster environment and parents require more treatment than the patient, as a rule.

**Trichoclasomania** is like trichotillomania, but the patient picks at and breaks off the hairs instead of pulling them out (Sutton J 66 195 1916)

**Onychotillomania**.—The nail is damaged by picking at it.

**Dermatothlasia** is a morbid state in which the person has an ungovernable desire to rub, scratch or irritate the skin of one or several parts of the body

**Factitious Dermatitis** is the title applied to injuries of the skin which are purposefully self inflicted, usually to excite sympathy gain compensation, or escape duty The lesions appear suddenly and range widely in character and distribution. As a rule they are sharply defined, asymmetric and irregular in outline and are located on a part of the body readily accessible to the patient Damage may be done by simple friction or by applications of lye acids, other caustic or irritating substances, hot metals or pointed instruments.

The peculiarities of the manifestations and the persistence of the eruption are valuable differential diagnostic points. The lesions are characterized by their want of similarity to a genuine disorder Straight edges, abrupt angles, and suggestive distribution are among the diagnostic features. Phobias and malingering are different problems (MacCormac BMJ 2 1163 1937) Care must be taken to exclude syphilis,

tuberculosis, dermatitis herpetiformis, acne varioliformis lichen planus, and chronic streptococcic ulcer In suspicious cases the patient should be secretly watched until positive evidence of guilt is secured then the patient should be told, privately firmly and quietly that the truth is known Sometimes the use of fixed dressings, which prevent further



Fig. 418.



Fig. 419.



Fig. 420

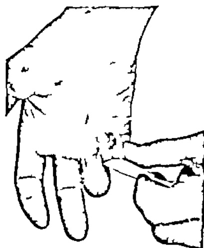


Fig. 421

Fig 418 —Tic of palpation

Fig 419 —Lip sucking (Dr Sam Sweitzer)

Fig. 420 —Trichotillomania.

Fig 421 —Delusion of parasitism the patient demonstrates her method of removing "worms" from her fingers

injury to the part is helpful in diagnosis as well as curative Eaton and O'Leary (ADS 36 544 1937) utilized the soporific state induced by giving Sodium Amytal during the effect of the drug it may be easier to obtain the patient's admission of guilt The plea for psychiatric management of these cases voiced by Bernstein (JNervMentDis 87 1 1938) will



Fig. 622.



Fig. 623.

Fig. 622.—Sores and scars from infections following injections in an opium addict. (Dr Anstruther Davidson.)

Fig. 623.—Injuries self-inflicted by squeezing skin to allay headache, by a Bataan native. (Dr Robert Simons.)

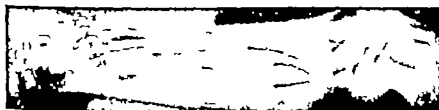


Fig. 624.—Lesions self-induced by liquid phenol.

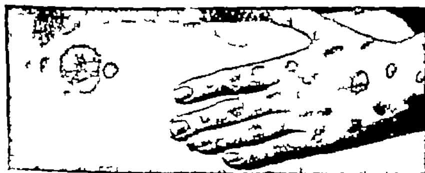


Fig. 625.—Scars of burns self-inflicted by a psychoneurotic teen-age girl.

hardly go unheeded Psychiatrists are welcome to them after a dermatologist has made the diagnosis. Corneal and pharyngeal reflexes are regularly absent (Graham and Lewis NYSJM 44 621 1944)

**Delusion of Parasitosis (Acarophobia)**.—The affected person believes he is infested with some parasite He will pick or rub off small particles of epithelial débris *and insist that the masses are or contain offending organisms.* The disorder may succeed upon an itchy organic disorder or develop independently Innumerable negative examinations of the material make no impression whatever upon the patients, but leave them no less firmly convinced that their integument is inhabited by a new species of small but exceedingly industrious creatures which will eventually prove their undoing *The forcible removal of a few of the outermost corneous* layers usually has a soothing effect on their minds, and after they have carefully destroyed the material and its supposedly dangerous contents, they are at ease until a recrudescence occurs. The majority of patients are women The condition is extremely difficult to combat successfully Its management constitutes a problem for the alienist

Phobia is misapplied in designating such conditions, according to Wilson and Miller (ADS 54 39 1946) for the patient is deluded but not fearful This is a symptom complex not sharply delineated from other delusions It may occur in toxic psychoses, paranoid dementia precox, involutional melancholia and paranoid states. The prognosis depends upon the variety of underlying mental error being more favorable in toxic and involutional psychoses and extremely poor in paranoia We can occasionally keep the patient from damaging herself by pointing out to her that external medication has done her no good that the offensive agent may be attacked internally with a hope of success, and that injections may render her body uninhabitable she then receives an occasional shot of B complex or estrogen and is perhaps happier and better off

Before fixing the diagnosis, one must be certain that infestation with the avian itch mite (q v ) or comparable inconspicuous irritant is not at fault (See also Filariasis, Paresthesia )

**Other Delusions.**—Klauder (J 85 1683, 1925; ADS 37 630 1938) reviewed the cutaneous neuroses exhaustively including bleeding stigmas, pruritus cured by psychotherapy (preferable in our opinion to irritant medicines) acarophobia and neurotic excoriations. He described erythrophobia, the fear of blushing syphilophobia (see Cormia CanMAJ 39 361 1938); rupophobia, fear of dirt, commonly resulting in traumatic and chemical dermatitis peladophobia, fear of baldness bromidrosiphobia, fear of being offensively malodorous topalgia, local pain of psychopathologic nature and cancerophobia, fear of cancer

## PRURITUS

Pruritus is defined as the symptom itching Many dermatoses are itchy and itching symptomatic of diseases described elsewhere in this book will receive mere mention, or not even that.

Idiopathic pruritus is itching due to causes of which the diagnostician is *ignorant. Pruritus as here used refers to states* in which this symptom is the main one provocative of excoriations and other lesions, but not caused by them The primary symptoms are itching burning tingling and formication Secondary manifestations, such as hyperemia laceration infiltration, lichenification pigmentation, secondary infection, and lymphadenitis, develop as a result of scratching and parasitic complication.

Itching may be constant or intermittent. The disorder may involve one or several regions, or even the entire skin. Exposure to heat or cold in persons with temperature sensitiveness will excite an attack. In the type known as bath pruritus, the burning and itching come on immediately after bathing and are usually due to contactants, the irritation of which is exacerbated by warmth. Soap is itself often the cause. Domestic cooking may incite pruritus in heat-sensitive housewives, although allergy to kitchen fumes from fuel or food may underlie such attacks. The desire to scratch is almost irresistible and the objectively normal skin soon presents rough and even bleeding areas.

In the generalized cases the entire surface is seldom attacked at one time but the sensations develop first at one point and then at another, skipping about disconcertingly without appreciable cause. The common generalized variety is that occurring in persons of advanced age, pruritus senilis. This may respond to testosterone by mouth (Dobes et al. J Clin Endocr 5 412, 1945). It is probably a result of vascular and atrophic changes in the skin. Pruritus is associated with jaundice; the deeper the jaundice the worse the itching. Preicteric pruritus occurred in 40 per cent of cases of Hoagland and Shank (J 130 615 1946).

The anal and genital regions are the parts most frequently affected in localized pruritus. While the disorder can occasionally be traced to mycotic infection, trichomonad infestation, dermatitis venenata from medicinal or other contactants, varicose veins, fissures, kraurosis and other local pathologic conditions, it is sometimes extremely difficult to locate the cause.

Pruritus vulvae ... common in pregnant women. Pressure and venous congestion are supplementary causes, and mycotic vulvovaginitis is common. Nail lacquer, soap, and perfumed powder are contactant causes.

Pruritus scroti is usually confined to the scrotum proper, although the shaft of the penis and the perineum are occasionally involved. An eczematoid condition may develop with thickening, redness and oozing. Dermatomycosis, dermatitis venenata, and scabies are the usual causes. Match box, clothing, soap, or metal dermatitis is the sort of thing to suspect.

Pruritus ani is an exceedingly distressing ailment. The anal, perianal, or intra-anal regions may be involved. Fissures and hemorrhoids are frequently although not invariably present. Irritation, thickening and induration, maceration, and even eczema, may develop secondarily. Contactant irritation is the usual main factor but fecal material is not, we think. Pinworms may cause it, and leakage of mineral oil is often a factor. Mycotic infection of the crotch (and feet) is commonly the cause in pruritus of the pudendal and perineal regions in members of either sex. Pediculosis, staphylococcic folliculitis, and toilet seat chemicals such as Lysol and chlorine are possible causes. Diabetic urine promotes bacterial growth, and insulin helps in pruritus of diabetic origin (Rudy and Hoffmann NEngJM 227 893 194 ). Psoriasiform seborrheic dermatitis, *lichen sclerosus, and lichen simplex chronicus* ... are other dermatoses of the region.

Pruritus hiemalis and pruritus aestivalis are peculiar recurrent types which develop with the advent of winter and summer respectively. Pruritus hiemalis is more common. The attacks occur as a rule at night when the patient is disrobing, or in the morning when he arises. The paroxysm of itching lasts for an hour or more. It finally dies down as the normal temperature of the skin is regained.

Pruritus of psychogenic nature is discussed elsewhere.

**Etiology**—Tangible factors are changes in the skin such as occur in old age, jaundice, hyperthyroidism, glycosuria, oxaluria, gestation, intestinal parasitism, lymphoblastoma, and intolerance of drugs (see dermatitis medicamentosa). In localized pruritus, a causative factor can usually be unearthed. Local causes include fungi, roundworms, constipation, stasis due to gestation, hemorrhoids, fissures (streptococcic?), kraurosis, dermatitis from medication (a common and important factor), dermatitis vene-

nata of other sources, and lesions of lichen planus and other pruritic dermatoses. Itching due to fungus or trichomonad should readily be recognizable as such. Inconspicuous mycotic vaginitis may maintain an almost ineradicable monilial intertrigo with attendant pruritus. Inconspicuous interdigital or nail infection with *Trichophyton*, *Epidermophyton* or *Monilia* may keep reinfecting the pudendal skin. Allergy in any of its forms may provoke itching. Gases or dusts may act by respiratory absorption as well as by contact. Some cases are submacroscopic contact dermatitis. Soap, clothing (wool, silk, fabric finishes), cosmetics (including scented talcum and nail lacquer) and medicinal agents are to be suspected (see dermatitis venenata). Olive oil causes pruritus in some cases. Pressure and posture may be concerned in some cases. In cardiac decompensation, the skin of the back, where the patient rests on it, is likely to itch simply from inadequate oxygenation; the same cause underlies the itching produced by a girdle. Pruritus is a significant symptom in the lymphoblastomas.

**Treatment.**—If possible, the cause should be located and removed. Generally speaking, the diet should be simple and nutritious. Alcohol and coffee are likely to prove harmful. Alkalinization is worthless. Internal remedies often alleviate the discomfort. We have lost faith in bromides, which are prone to intoxicate. Aspirin is more suitable and is almost always harmless. Nervous patients with flabby dry skins often need thyroid extract or vitamin A concentrates or both. The vicious cycle of insomnia, sedative, coffee to excess, more pruritus, insomnia, sedative and coffee is commonplace. It eventuates in exhaustion and drug intoxication. Banks (J 100: 328, 1933) recommended subcutaneous injections of histamine, in doses of 0.5 mg. twice daily in pruritus and urticaria. Foreign protein shock often proves helpful. Small doses of potassium iodide give relief in some cases of senile atrophy with itching.

The antihistamine drugs are often quite successful in palliating generalized pruritus. Antistine 100 mg. with meals and at bedtime may be suggested.

For intolerable itching MacCormac (BMJ 2: 48, 1946) considers the temporary abolition of the urge to scratch by sedation with intravenous Novocain 0.1 per cent 1 000 c.c. in 2 hours daily, or continuous narcosis with Somnifaine may be tried. Beinhauer (TransADA 1947) described the use of tribromethanol (Avertin) 60 to 100 mg. per kg. for 6 or more days in the alleviation of desperate pruritus in various conditions. Ethyl alcohol 5 per cent in isotonic saline, may be used intravenously in doses of 500 to 1 000 c.c. of the dilution with little hazard and good temporary narcosis. A grain of papaverine hydrochloride may be given slowly intravenously, yielding 1 to 6 hours of respite (Wirth, JInvD 8: 63, 1947). Epstein (ADS 53: 281, 1946) acknowledging the hazards, used aminophyllin 0.5 gm. in 20 c.c. water intravenously for similar purposes.

In patients in whom attacks of itching are provoked by heat, effort and emotion, there are those who respond with urticaria and those who suffer generalized pruritus without urticaria. The urticarial group differ from patients with other varieties of urticaria in that attacks can be provoked by injections of derivatives of acetylcholine (Grant et al., ClinSc 2: 253, 1936). Nomland (ADS 50: 247, 1944) described patients of the type who itch when influenced by warmth but are not urticarial and he observed the experimental precipitation of attacks by injecting intramuscularly into them 12 mg. of Mecholyl chloride. Attacks would start within 1 to 10 minutes and could be relieved by dousing the patient with cold

water In treating any pruritus, we frequently prescribed cool moist towels to be laid on the parts or prolonged baths or showers in water of such a temperature that it feels cool to the patient s skin.

External treatment is of great importance in all types of pruritus. The underclothing must be soft and nonirritating Old cotton and linen are preferable In laundering all soap should be rinsed out. Frequent bathing particularly in hot soapy water is to be avoided. Bran starch, and oatmeal baths are sometimes helpful in generalized pruritus, particularly if the skin is carefully dried afterward by patting and a bland dusting powder applied. Recourse may be had to carbolized calamine lotion

℞ Phenol ______ 1.0
Zinc oxide
Starch
Calamine ______ 20.0
Glycerin ______ 10.0
Water ______ 180.0
Sig Shake and apply freely to allay itching

One must be alert to the possibility of intolerance of even simple and generally innocuous agents, especially menthol. Calamine is unsuited for long usage by the xerotic individual Petrolatum or mineral oil is preferable to cold cream or olive oil. The following prescriptions for topical antipruritics may be useful (see also chapter on treatment p 46)

℞ Camphor, powdered ______ 2.0
Zinc oxide,
Cornstarch,
Zinc stearate______of each, to make 60.0
Sig. Dusting powder for relief of itching

℞ Potassium permanganate______ 30.0
Water______500.0
Sig.: 3h to 15 gallons f tepid water for baths daily or twice daily for 15 minutes.

℞ Phenol______ 0.3
Salicylic acid______ 0.3 0 6
Zinc oxide,
Cornstarch______ 4.0 8 0
Petrolatum______to 30.0
Sig. Bland paste f relief of itching. Wet applications may be superimposed as ordered.

℞ Ethyl aminobenzoate (anesthesin)______ 3.0
Lanolin______ 4.0
Petrolatum______to 30.0
Sig Anesthesin ointment t stop local itching.

℞ Phenol______ 4.0
Potassium hydroxide 5%______ 4.0
Linseed oil______t 30 0
Sig. Brocq's alkaline antipruritic oil to remove scales from localized lichenoid lesions.

Ointments containing 2 per cent coal tar 2 per cent ammoniated mercury or even 10 to 25 per cent calomel, occasionally are of service in parasitic pruritus. A 10 per cent camphor-chloral hydrate ointment is helpful in some instances. Applications of folded cloths wrung out in either cold or hot water often relieve. Cleansing should be accomplished by water alone without any detergent.

Reviewing the physiology of the sensibilities, especially itching, Bishop (JInvD 11 143 1948) noted that itch can be induced by the summated effect of weak electric shocks individually below the threshold of pricking sensation itching he believed results from a particular pattern of stimulation of pain endings. The nerve track of the itch-scratch reflex interested Koenigstein (ADS 57 828 1948) whose experiments indicate the existence of a scratch center in the lower part of the medulla oblongata. While ergot or yohimbine prevented or suppressed the itch-scratch reflex induced in various ways, they did not influence it when it was induced by irritating intracisternal injections. In itchy human beings, injection subcutaneously of 1 mg of dihydroergotamine (capable of doing harm see p 105) may allay itching

In anal and vulvar pruritus, a cause can generally be found, and purposeful treatment rather than symptomatic can be chosen Cervical erosions and trichomonad infestation must be dealt with. Treatment by tattooing with cinnabar is an interesting enterprise, which helps some patients (Turrell and Marino AnnSurg 115 126 1942) An ointment containing estrogen may benefit the patient with pruritus of kraurosis (q v ) Employment of anesthetizing substances by injection or the sectioning of nerves is rarely prescribed by dermatologists, but surgeons, being less resourceful with topical efforts, frequently resort to such methods (Steinberg NEngJM 215 1019 1936 Swinton SCNAm 19 689 1939) The scrupulous hygiene recommended by proctologists often results in soap dermatitis. Dietary restrictions, popular with proctologists, seem rarely consequential to us. A powder we have found helpful in anal itching consists of equal parts of bismuth subnitrate and zinc stearate. Korth tells us that proctoscopic examination in pruritus ani often reveals rectal inflammatory puncta, and that in such cases the instillation of mercurochrome solution a dram to the ounce of water is beneficial

All cases of pruritus demand investigation of etiologic factors, which *can generally be found. Treatment cannot be standardized* Pruritus is as bad a final diagnosis as eczema

## INFANTILE DERMATITIS

**Symptoms.**—Itching is the initial manifestation. The infant scratches with every means at its command. There successively develop erythema and papules, oozing crusting and secondary infection. The flush areas of the cheeks are the sites of predilection, and the forehead, ears, scalp extensor surfaces of forearms and arms, and legs and thighs are likewise often involved. This description fits such cases as are said usually to be due to food allergy. Another type is characterized by the appearance of circular and oval plaques of yellow red minutely vesicular dermatitis, marginated and with predilection for the napkin area. This can spread over the trunk and may become almost universal. Impetigo and infectious eczematoid dermatitis of the newborn (p 161) are streptococcic and staphylococcic parasitism. Infantile eruptions clearly dependent on foods are sometimes acneform with or without actual pustulation, and respond promptly to diminution of lipid rich substances and oily vitamin concentrates.

Dermatiti in a baby cannot long persist without becoming secondarily infected with parasites capable of arousing sensitization just as occurs in adults. In any case in which cure is not promptly forthcoming the disease is likely to become chronic and persistent, rebellious to treatment and prone to undergo relapses and recurrences. Extension of dermatitis from the cheeks may come to involve progressively larger areas, the head, arms, legs even the entire body. Such pitiable patients may be universally exudative exhibiting general lymphadenopathy and a white blood cell count so high as to suggest leukemia although it is actually inflammatory while serum proteins are depleted and red cells so reduced that transfusions are essential. Multiple abscesses, bronchopneumonia and gastro-enteritis may terminate the case mortality being estimated at from 4 to 14 per cent (Glaser and Edwards AmJDisChild 60 526 1940). Flares appear to be associated with high unsaturation of plasma lipids (Stoesser JAllergy 13 ?48 1949). Milder disease is fortunately more common and there is a tendency, upon which one should not rely too confidently, for dermatitis to fade as the child grows older.

Urbach (Nutrition and Metabolism, Grune & Stratton 1946) described (1) the overnourished f t child, who improves when the milk is cut down; (2) the d trophic, marasmic enteritic infant with dry eczema who improves when the diet is improved; (3) the exudat v patients w th rest on the scalp and face who g on t ha atopic dermatitis, and are allergic to milk and (4) cases of unknown etiology which are not helped by diet ba ges. I bach and with commendable candor gara and again failure has awarded m sincerest ffort t help these children. Foerster (JOklaMA 30 290 193 ) divided the cases at seborrheic dermat tis afection dermatitis, mycosis and contact dermat tis and he eserved atopic dermatitis for the remainder. He found goat milk well tolerated a rule f cow m lk not Sova bean prepare tions may fa l because f an unsuspected lack content. I breast fed eczematous baby is likely to be sensit t egg. H ll (J ll 113 1939) believed that contactants ga n in importance in etiology a the hild grow older while foods are most important in infancy. He stated that the seborrheic type with and ement of the cheeks and scalp is likely to respond t diet n treatment. He found that of 1?6 cases actually sensiti t milk, 104 had their onset before 6 months of age and 3_ before 3 months. f sensit ity is t the casein fraction heating the milk will prove use a ling but in tolerance of casein is not as common a intolerance of lactalbumin which is readily

altered by boiling If boiling fails to render the milk tolerable, evaporated milk, goat's milk, or a proprietary (S.M.A. hypoallergic milk) may be tried. Hill's failures, he said, occurred in severe generalized cases. Elimination diets are given in detail by Cobb (AmJDisChild 50 18 1935)

Scurfy scalp in infants may be divided into 3 types, according to Gordon (BMJ 1: 183, 1940) (1) milk crust due to lack of soap and water [illegible] of mothers to rub the scalp hard over the fontanelle and application of oils (2) true *dandruff* an *infection acquired from the mother*; (3) mixed, comprising both of the others. When a child has dandruff and gets dermatitis due to atopy or contact, the scaling disease of the scalp may spread to complicate the whole.







Figs. 436-438 —Infantile eczema.

**Etiology**—Dermatitis in infancy like dermatitis in adults, is hardly to be ascribed to one agency in all cases (Silvers and Coe JPed 16 160 1940) The dermatologist sees so many infants whose diets have been juggled as the sole effort toward curing what was in fact scabies, contact dermatitis, or coccic parasitism that he tends to discount food intolerance almost as emphatically as the average pediatrician stresses it In some cases, however real food allergy exists. It is best detected by limiting ingesta to one substance for a few days, observing improvement then feeding suspected foods one after another systematically observing that trouble follows the ingestion of certain of them Skin tests yield falsely positive and falsely negative reactions more often than they yield useful information, so that competent allergists tell us they employ skin tests to satisfy a demand rather than to enable themselves to aid the patient Milk is the commonest single offender wrote Bain (SMJ 34 863 1941) Evaluating elimination diets in 198 cases, Birt (CanadMAJ 42 520 1940) reported eggs worst, then tomato orange juice milk, fish, oatmeal, and cod liver oil.

Elements of contactant mechanical and chemical intolerance and autoinoculated coccic parasitism are usually underestimated in interpreting these cases. Even mild agents which may give negative patch tests may be intolerable when long used widespread on the body. Silk, wool, and rayon are common sources of irritation. Mild food allergy and severe medicinal contact dermatitis are likely to be combined. Greatest offenders are fabric finish, soap, unguents (including baby oil and olive oil) and environmental agents, such as mattress stuffing; less often the agents are associated with the parents' clothing (finish, dye) or cosmetics (nail lacquer). Human dander may be an important contactant (Simon, J 125 350 1944). Ammoniated mercury accounts for a fair quota, and tar in too great concentration is an irritant. Any salve smears staphylococcic about and enhances their pathogenicity.

**Treatment.**—Many writers have stressed the necessity of preventing scratching. Arm splints made from cardboard tubes are useful, and at times restraint must be employed. The maintenance of a proper nutritional balance is essential, and if this is successfully accomplished, recovery is to be hoped for. During food testing, orange juice, tomato juice, and cod liver oil should be *temporarily* discontinued. A quarter of an aspirin tablet may be added to each milk feeding for sedation. While skin tests are unreliable, antibodies demonstrable by passive transfer technic may be important guides. A basic diet consisting of soybean emulsion (Levin, JPed 17 79 1940) or of foods to which scratch tests are negative, may be given. It is supplemented one food at a time at intervals of several days until offending and harmless foods have been distinguished and a full diet has been designed. Cevitamic acid may be substituted for orange juice. It is a grave error to allow an eczematous baby to endure malnutrition long. If a food actually is intolerable, it must be totally avoided. Heated goat's milk, rice, cane sugar, and vitamins and minerals are usually trustworthy (Cline, WiscMJ 40 789 1941). Interesting hypotheses regarding the role of fatty acids in nutrition have led to reports of benefit from feeding lard by such authorities as Hansen et al. (AmJDisChild 73 1, 1947).

Investigations of contact and environmental allergens made possible most of the satisfactory results of Osborne and Walker (ADS 38 511 1938). The first attack in treatment is the elimination of contact and environmental allergens, and this alone cured half of their cases, and helped two-thirds of the remainder. Mineral oil and petrolatum, cornstarch, cotton, and water are safe; nothing else is. The baby's external environment should be limited to these, with the implication that those who handle the infant should be free from cosmetic and toilet articles and should wear unstarched cotton house dresses. Removal of drapes, carpets, furniture and toys is sometimes ordered, usually by physicians who are comparatively amateur in controlling contactants and who neglect to interdict soap.

Locally a mask tied over the face and head serves to keep in application a wet pack of 0.2 per cent aluminum acetate, or a mull of Lassar's paste or of 1 per cent crude coal tar in a zinc oxide, starch, and petrolatum vehicle. Gentian violet in 1 per cent aqueous solution is an excellent antiseptic to be used in conjunction with wet dressings, and tragacanth lotion serves as a cleansing agent. Clothing should be loose and cool, for warmth incites pruritus. The skin may be intolerant of all oily substances, and ointments do not succeed when coccic complication exists. Blood or plasma transfusions may be indicated (Wolpe, CalWM 67 156 1947). Peni

cillin given with the formula may effectuate the elimination of cocci. Sodium Amytal a 1 grain capsule with a hole pricked in it and inserted into the rectum may prove useful in sedation, and Pyribenzamine or Benadryl afford some palliation at times.

## ATOPIC DERMATITIS

**Symptoms** — Atopic is an adjective applied by Coca and Sulzberger (Sulzberger Dermatologic Allergy Thomas, 1940 p. 158 ff) to designate a type of sensitization characterized by a familial tendency to the development of certain forms of disease, principally hay fever asthma infantile dermatitis, and a chronic relapsing rebellious lichenifying dermatitis which differs distinctively as a clinical entity from other dermatoses. In atopy' one observes in a family the common occurrence of urticarial reactions to skin tests, demonstrable reagins, and the above listed disease forms Atopic individuals in an incidence significantly higher than other individuals evince these particular and peculiar abnormal forms of allergy which differ from ordinary acquired sensitivity and from intolerance of contactants. Atopic dermatitis is to be recognized as the childhood and adult manifestation of infantile eczema which is itself atopic rather than the precursor of atopy (Hill and Sulzberger ADS 32 451, 1935) Hay fever and asthma usually precede, but may accompany or follow atopic dermatitis in one individual

The typical case of atopic dermatitis exhibits symmetrically distributed, chronic inflammatory thickening of the dermis, fine and uniform scaling, exaggeration of the minute folds and grayish brown hyperpigmentation. Areas of predilection are the head face, neck, upper chest and back, and the flexures of the elbows and knees The upper half of the body bears the brunt of this dermatitis, although in extreme exacerbations involvement may become almost universal. The surface is generally dry but may be considerably excoriated because of the severe and characteristic pruritus Hair is not lost but may be rubbed off Flares and remissions mark the course which is extremely chronic Patients are generally worse in winter months and better in the summer Flares are unpredictable and are marked by extension of involvement increase in pruritus and swelling of the dermis until perhaps exudation is severe and widespread Remissions may be complete or almost complete One is likely to attribute remission to the last treatment tried, only to find when the next exacerbation takes place that this seemingly promising medical effort fails. As the sufferer grows older the disease apparently abates, for the clinician seldom sees such patients past middle age Perhaps they have learned to care for themselves as expertly as physicians can care for them and have given up the struggle Sometimes the disease disappears for months or even years. When it does, one seldom knows why but patients sometimes hit upon a climate or way of life which allows them to maintain well being When the disease is active secondary infection and chemical insult from inappropriate medication are likely complications.

**Etiology** —The disease is believed etiologically to rest on hypersensitivity Of 101 cases Brunsting (ADS 34 935 1936) reported that 71 had had infantile eczema hay fever or asthma. The age range was 15 to 35 years, and there was no predilection as to sex Ten cases were complicated by juvenile cataract Cataract complicating atopic dermatitis is not rare (Beck ADS 39 604 1939 Mitchell ib 41 402, 1940) Keratoconus affects 12 patients of Bereston and Baer (ADS 46 358, 1942)

The natural evolution of allergy during the life span was reviewed by Ratner (J 111 2345 1938) While the onset may be early the newborn period is signally free Eczema is the prevailing symptom of allergy in infants less than one year old, and foods are the prevailing reactive substances. In his series, 59 per cent of allergic dermatoses were due largely to contact with environmental substances to which the infants reacted. The age of onset of dermatitis precedes asthma and dermatitis is often the forerunner of asthma After early infancy asthma is the prevailing symptom of allergy Food sensitizations play an important role in allergy in childhood but so also do inhalants and contactants. Multiple reactivities suggest that specific therapeutic measures may fail if all offenders are not taken into account.

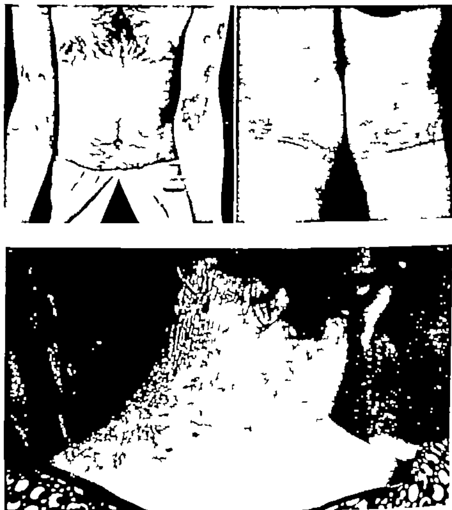
Atopic dermatitis Sulzberger and Goodman (J 106 1000 1936) considered to be specific vascular skin hypersensitivity to food or environment l allergens. Despite insistence on the etiologic relationship of sensitization, no dependable therapeutic results are obtained by removing from the environment of the patient all the llergens to hich he tests positively The individual is believed t have become sensitized in infancy so as to manifest infantile dermatitis at that period of life hi sensitivity then becoming polyvalent and so diffused that almost no environment is possible wherein no sensitivity exists or may develop. The term environment is mea t in the broa lest sense to include foods and inhalants a well a plants, animals, and mat rials. It is, however of benefit to remove as many recognizable irritants as possible.

[Magnesium deficiency results in a dermatitis in rats, and spectrographic in lications of magnesium deficiency in atopic dermatitl ha e been reported (Engman and MacCardle ADS 46 337 194_) But the rat disease loes not resemble the l uma and magnesium therapy does ot help the patient acco d g t Sullivan and Evans (ADS 49: 33 1944).]

Disseminated Neurodermatitis is same for this disorder although Sulzberger and Goodman (1936) discovered no convinci g evidence of psychoneurotic etiology in their study of 60 cases. In some cases there ppears to ex st t least a come lence of increased tension and flare Psychiatric studies by Greenl ll nd P ason ger (ADS 46: 187 1942) and Lynch et al. (ib. 51: 31 1945) ha e revealed feelings f h stility inadequacy and depression and inherent ons of psychobiologic mbalance: The mood tended to be grudging sorrowfully serious a tendency tow rd st bborn rigi l ty and high emotional reacti ty masked l y suppressio Of dermatoses and neurosis which is cart and which is horse a question. What h lps the adult ought t help the infant with the same disease, and this is true of such ffort as liminat g contactant and in gestant provocations, but is not true f psychotherapy Where fact l lacki g, an opinion may be held W do ot belie in neurodermatitis. Yet Wals and Kierland (PSMMC 22 578, 1947) helped patients who permitted several month f hospitalization more when they t lized psychotherapy than when they limited their fforts t accepted dermatologic measures. See A kermann (PsychosomM 1: 366, 1939) Saul (ib. 3 66 1941) Pearson (ib. 2 22, 1940) The i telligence f the allergic child is probably neither ret rded nor advanced as compared with the normal (Chobot et al. AmJDisCh ld 57 831 1939)

**Treatment.**—The first accomplishment must be the elimination of contact irritants, and of these friction soap wool and unsuitable medicines are the most important This measure is likewise first in infantile dermatitis. Cleansing is to be done with wat r alone without a washcloth for friction is harmful so that starch t should l be left out of the clothing The safest topical application is petrolatum When any grease is applied thick in the ordinary way the kin feels better for a few minutes then commences to prickle and tingle yet the sensation of dryness calls for a grease. The patient may find com f rt in applying the ointment then taking a warm shower to remove the excess, then a cool rinse to quiet the itching provoked l y warmth The same amount of xeltation arising in

the skin is better tolerated by the patient if he is relaxed and rested. He should avoid overfatigue, coffee, and tea and anxiety in so far as he can be taught to do so. Psychotherapy to this extent must be admitted helpful. He should sleep in a warm room with few bedclothes, thus keeping the skin cool. In a paroxysm of itching a tepid bath will allay, or a towel moistened with cool water and applied to the itchy parts. Mild sedation, such as 0.3 gm. aspirin each 3 hours, and an occasional Seconal at night has its place. Benadryl and Pyribenzamine may be tried and benefit accrues in about half the patients.



Figs. 629-631.—Atopic dermatitis ("neurodermatitis") as seen in three individuals. (Becker and Obermayer, *Modern Dermatology and Syphilology*, Lippincott, 1940.)

Elimination of intolerable foods is the next step. Sometimes this is therapeutically highly remunerative. The single food additive technic described for urticaria (p. 115) is as simple and successful as any (compare Flood and Perry, ADS 55, 493, 1947). A paroxysm of itching may be expected to follow the ingestion of a food allergen within a few hours.

Elimination of all such foods and of contact irritants has been known t relieve patients considerably Inhalants were important in the seasona cases of Feinberg (ADS 40 200 1939) and desensitization was worth undertaking

Elimination of focal infection and secondary infection is indicated. Teeth, tonsils, and genitourinary organs should be freed from disease Penicillin helps greatly in this effort

Skin tests are of little use although the scratch and passive transfer tests may afford some assistance (Goodman NEngJM 219 705 1938 Rusten MinnM 23 16 1940) Human dander rubbed onto scratches provoked the development of patches of the disease reported Simon (ADS 51 402, 1945)



Fig 632



Fig 633

Fig. 632.—Atopic dermatitis (Dr Clyde Cummer)
Fig 633.—Lichenoid dermatitis, lichen chronicus simplex of nucha

Topical therapy with the usual bland agents, boric acid, aluminum acetate, and the like is used Chrysarobin ointment in 1 to 2 per cent strength, may help a chronic stubborn area for the skin is comparatively tough and immune to irritation in this disease wrote Wise (NYSJM 33 1321 1933) Weak coal tar ointment is often prescribed. Sunshine or ultraviolet light has a place some patients are helped by a coat of tan A move to a different geographical location sometimes brings about relief. A warm, dry climate seems preferable X ray therapy in cautious dosage will alleviate the symptoms.

All sorts of efforts have been tried with occasional seeming benefit fever therapy autohemotherapy injections of arsenic histamine desensitization (to which reaction may be severe Smith ADS 44 863 1941 Costello Ib 53 309 1946) liver extracts and vitamin injections (Marchmon Robinson UrtRev 4- 912 1936) etc See discussion (ADS 53 658, 1946) No physician feels secure in his management of atopic dermatitis.

## PRURIGO

**Prurigo** is the name for a persistent dermatosis characterized by intensely itchy papules occurring especially on the extensor surfaces of the limbs. It is probably a form of atopic dermatitis which it often accompanies. (White: OutAGUDs 13 –, 189 ) Antihistamine drugs may effectively palliate.

**Prurigo Nodularis** is a rare, chronic dermatosis characterized by discrete firm, nodular persistent intensely itchy tumors which are usually scattered over the legs and arms. Most of the patients have been women, between the ages of 23 and 50. The lesions are pea- to hazelnut-sized, smooth, scaly or verrucose nodules irregularly scattered and accompanied by intense itching. The onset of the disease is usually gradual, and the affection is an exceedingly chronic one. The surrounding skin is generally thickened and fibrotic. Removal of the growths has occasionally been followed by recurrence. The tumors range in number from 30 to 60 or more. They seldom coalesce. When fully developed they remain stationary for years. See Netherton (ADS 8: 183, 1923).

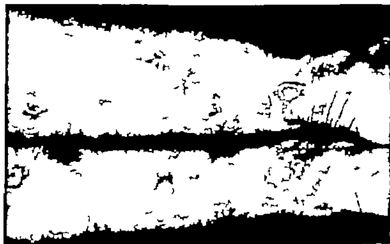


Fig. 614.—Prurigo nodularis.

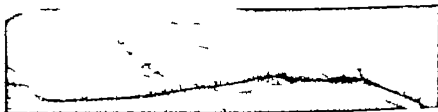


Fig. 615.—Prurigo. (Dr Arthur Hertzler.)

The cause is unknown. Pautrier (abs YBD 1925, p. 463) studied sections prepared with Mallory's trichrome stain, which revealed that the infiltration consists of lymphocytes, histiocytes, some mast cells, and a few plasma cells, that the vessels are numerous, tortuous, and infiltrated, and that there exists in the center of the nodule to periphery or even encircling it, neuroma-like masses of hypertrophied nervous tissue. Large nerves were seen, the fibers sheathed with collagen.

Permanent relief cannot be promised but something can be done to alleviate the discomfort and, as a rule, many lesions can be eradicated. Brunsting's oil, which consists of 15 per cent each of phenol and liquor potassii hydroxide in olive oil, is valuable. Cycloform, 25 per cent in petrolatum, also is good. Andrews recommended

excision by means of high-frequency cutting current, followed by roentgen therapy. In one of our cases, prolonged freezing with solid $CO_2$ gave considerable relief although the reaction was severe, healing was slow, and many lesions so treated recurred. In another case the lesions were excised and the wounds allowed to granulate. Lesions so treated remained cured, but the patient gave out before her nodules did. No lasting benefit ensues from roentgen therapy if the dose is less than necrotizing.

## CHRONIC DERMATITIS OF UNKNOWN CAUSE

**Confusing Exudative Dermatitides**, once called "eczema," are described under streptococcic dermatitis, staphylococcic dermatitis, dermatitis venenata secondarily infected, and dermatomycoses and dermatophytids. See Dermatitis venenata, complications, p. 91. Having distinguished these conditions, little remains of the classic but outmoded diagnosis of "eczema."

When dermatitis persists, the practical attack may be based on the presumption that something interferes with healing, for the tendency to heal may be trusted. The search for interfering agencies must take into consideration contactants, secondary infection, focal infection, food allergy, mechanical factors, psychosomatic problems, and inadequacy of tissue nutrition which may be due to defective circulatory, nutritional, endocrine, kidney, liver or hematopoietic function. It is usually possible to eliminate such factors systematically and so to obtain cure or alleviation.

**Chronic Dermatitis of the Hands and Feet.**—This topic is also considered under the title, Recalcitrant Pustular Acrodermatitis (p. 179). In such cases we stress the elimination of contactants first, then give attention to foci, in which effort consultations are required: dental films, extractions, and treatment for periodontoclasia, tonsillectomy, prostatic massages if pus is found in prostatic secretion and transurethral clearance of obstruction which maintains cystitis, and gynecologic help with erosions of the cervix and operative repair of cystocele which maintains cystitis. When these things have been done, accompanied suitably by sulfonamide therapy for pyuria or penicillin "coverage" of operative work, a high proportion of obscure dermatitides are cured. If they are not, the next step is elimination of food allergens following the technic of Flood and Perry (ADS 55: 493, 1947). These authors use a single food additive diet such as Winston uses in urticaria (q.v., p. 115), starting with castor oil and sugared water for 24 hours and followed by the ingestion of a new single simple food each day. We find it successful and expeditious to test a new food as often as each 4 hours, so obtaining a full diet in a shorter time. Elimination of food allergens by the method of Rowe (ADS 54: 683, 1946) is less practical. One notes exacerbation signalled by flares of itching, followed by redness and the appearance of new excoriations, for such phenomena indicate that the last food tested was intolerable. Such a food is withheld for a week or two, to be retested later. When the flare begins to fade in two or three days, further simple foods are added, one at a time, so that gradually there are built up lists of tolerable foods in adequate quantity and variety and of intolerable eczematogenous ingesta. Since we have been using these methods in our management of chronic dermatitis of the hands, we have approached such cases with confidence. See Stokes et al. (J 123: 195, 1943); Lane et al. (ib 128: 987, 1945); Winston (ADS 57: 357, 1948).

Herpetoid (Nummular) Dermatitis was studied by Pollitzer (JCut Dis 30: 716, 1912). It attacks the dorsal surfaces of the hands or other parts of the extremities. Round or oval patches appear 1 to 5 cm. in diameter, consisting of groups of vesicles or vesicopapules. The itchy efflores-

cence slowly recedes and heals, but may recur abruptly several times a year in approximately the same location. Worse in winter and aggravated by friction and alkali as a rule, the condition may be helped by administration of vitamin A (Gross ADS 44 1000 1941). It is recalcitrant to local medication, like pustular acrodermatitis, although x-ray therapy will cause its temporary disappearance. Improvement of most cases and cure of some were obtained by Schoch (JChemother 15 36 1938) by the use of sulfanilamide. *We think it not importantly different from other varieties* of chronic dermatitis of the hands.



Fig. 436.



Fig. 437.

Fig. 436.—Chronic dermatitis of the hand, impetiginoid and with x-ray atrophy.
Fig. 437.—Chronic eczematoid dermatitis of the hand.

**Leg Ulcers** comprise a variety of chronic dermatitis. As Luke (CanadMAJ 43 217 1940) wrote, there is a tendency to devote too much *time* on local treatment and too little consideration to etiology. The article of Callaway et al (SMJ 39 375 1946) deserves careful study. Leg ulcers are often associated with lichenoid dermatitis. In addition to efforts directed at such dermatitis, and at tinea of the feet if present (Marshall MTimes 75 154 1947), one has also a problem in tissue cultures, for the ulcerous defect must be filled with granulation tissue and recovered with epithelium. Surgeons tend to attribute too large a share of *causation* to stasis. Most dermatologists are incompetent to adjudge or treat the circulatory aspect of the disease. Leg ulcers occur in sickle cell anemia, but the lesions as such are not distinctive; the disease is familial (Woofter AIntM 76 230 1945).

In general, a leg ulcer should be treated in such a way as best to enable tissue growth and healing to occur. Then what is put onto the ulcer itself is a matter of indifference so long as it is not injurious, and cod liver oil, chlorophyll, red blood cells, pectin, silver foil, insulin, maggot juice, merely zinc oxide ointment or petrolatum are equally satisfactory. "When a topical agent seems to accelerate wound healing it does so by prevention or reduction of factors which tend to retard healing," wrote Sulzberger and Baer (YBD 1944 p. 449). Supportive bandaging or an Unna paste



Fig. 438

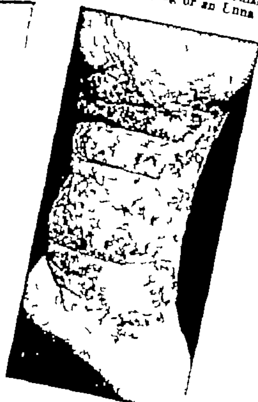


Fig. 439

Fig. 438.—Herpetoid eczema.

Fig. 439.—Chronic dermatitis of the leg. His varicosity, stasis, obesity, secondary infection, cystocele, and periodontoclasia.

boot is helpful (Fillmore, TexasSJM 35 281 1939; Zimmerman and Faller, SGO 70 792, 1940; Isaak, ADS 41 530 1940; Marbury and Jackson, VaMMonth 67 288 1940; Gordon, CanadMAJ 42 4, 1940). Penicillin by injection before and after grafting improves the likelihood of takes (Nomland and Wallace, J 190 663 1940). Vitamin intake and requirements must be considered (Maynard and Hollinger, J 121 1184 1943). Pratt (J 122 797 1943) gave clear instructions for the selection of candidates for varicose vein surgery; see also Ochsner and Mahorner (Varicose Veins, Mosby, 1939) and Allen et al. (Peripheral Vascular Diseases, Saunders, 1946 p. 666 ff).

**Tropical Ulcer.**—Many synonyms exist, including Desert Sore, Veldt Sore and Naga Sore. Authorities ascribe part of the etiology to high humidity or to dryness

depending on where they have seen their cases. It is a hot-climate and summertime disease as a rule. Patients often, but not always are ill nourished, malarial, or otherwise below par. Blood personnel may be more susceptible than the dark skinned natives (Henderson BMJ 1: 657 1943) The extremities especially the legs, particularly if these parts are unprotected by clothing are the usual location. A minor trauma or insect bite is the initial lesion, and there quickly develops a tense or flaccid bulla, its content at first clear or sanguineous, later purulent. Exactly beneath the bulla the dermis undergoes necrosis, so that a painful, punched-out ulcer develops. This enlarges slowly and remains a chronic and rebellious sore in which bacteriologic endeavor reveals variously Vincent organisms, staphylococci, streptococci, and sometimes *C diphtheriae*. See ecthyma (p. 173) diphtheria (p. 202) leishmanial oriental sore (p. 344), and local infection with gangrenous dermatitis (p. 183) The lesions may become large and deep even exposing bone. They are solitary or few in number. In the classic cases we have watched develop we have cultivated pure hemolytic *Staphylococcus* as cus from the early bleb and have thought the slough to be due to it dermonecrotizing toxin. If the earliest lesions are promptly and carefully attended, using gentle débridement, cleansing, and a tiseptic such as gentian violet ulceration is prevented (Vierber Abs YBD 1943 p. 305) After ulceration, there have been recommended permanganate compresses, cleanliness occlusive dressings sulfonamides, and intravenous arsenoxide. Penicillin is effective. See Hamberger (IndMGaz 74: 131 1939) Rapport (BMJ * 98, 1942) Bettley (Abs YBD 1944 p. 273) Costa (AD[a] 49 290, 1944) Fessman (NEngJM 231 475, 1944) Webb (BMJ 2: 49 1946) Golden (BMJ 40: 214 194 )

## LICHENIFIED DERMATITIS AND LICHEN CHRONICUS SIMPLEX

When chronic dermatitis consists of fairly sharply defined scaling, pruritic patches, the eruption is said to be lichenified. Papules bounded by the minute skin wrinkles are confluent in the central areas of the patches, while satellite papules are seen about the periphery. The color is brownish or yellowish and the texture is thickened. The surface is dry excoriated, perhaps secondarily infected and slightly scaly and is marked into little squares and diamonds. The patches may be symmetrically located. The sites of predilection are over the extremities, the trunk, and in women often the nuchal postauricular and occipital regions. Itching, which is persistent and may occur paroxysmally is severe.

Circumscribed lichenification sometimes starts with what appears to be infectious eczematoid dermatitis. This after a few months settles down as a nonexudative persisting lesion (ADS 52 47 1945) When such a dermatosis is irritated macerated or infected, there may occur what apparently represents absorption of some kind of toxic material, for an id like eruption puts in its appearance with acutely disseminating itchy lichen id dermatitis developing symmetrically and especially on the flexures of the wrists and forearms, the extremities, and elsewhere (Smith BMJ 1 628 1945) This rash quiets down and usually disappears when the primary lichen id lesion is treated with permanganate compresses. See Wise (JCutDis 37 590 1919) clarifying primary and secondary lichenification Cleveland (CanadMAJ 29 368 1933 ADS 33 316 1936) dubious of neurogenic factor Smith (BJD 54 255 1942) volar cases, distinguishing keratoderma climactericum

**Etiology** is little understood. Doubtless several different causes may produce lichenification. Pruritus and trauma due to scratching appear to provoke the histologic changes. Obermayer and Becker found the dermal reactivity variable as determined by scratch tests and posture in half the tests performed so that the response could be interpreted only as an underlying protoplasmic instability. The synonym neurodermatitis suggests the hypothesis held by some that a psychogenic factor is important; we do not believe this. Chronic contact dermatitis



Fig. 440.—Nummular dermatitis neurodermatitic reaction and vesicles (Miller AD&S 56 673 1947 )

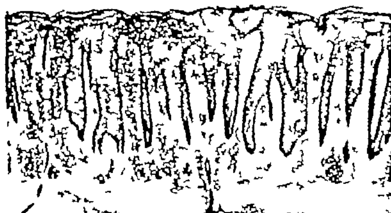


Fig. 441.—Chronic eczematous dermatitis irregular acanthosis, spongiosis, exudation and dermal inflammation (Miller AD&S 56 [illegible] 1947 )

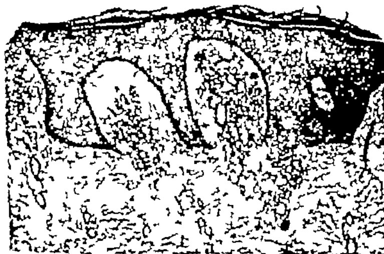


Fig. 442.—Chronic lichenified dermatitis of leg sclerosis, papillation, and acanthosis (Dr. Fred Waldman.)

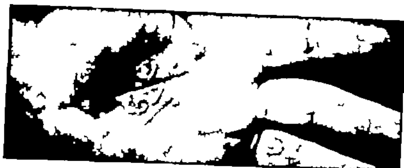


Fig. 645.—Erythema multiforme iris-like lesions of palm.



Fig. 646.—Erythema multiforme.



Fig. 647



Fig. 648

Fig. 647.—Erythema multiforme.

Fig. 648.—Eruptive fever with stomatitis and ophthalmia. (Glanzmann: Am J Dis Child 49: 1144, 1936.)



Fig. 140.—Nummular dermatitis neurodermatitis reaction and vesicles. (Miller ADM 56: 678 1947.)

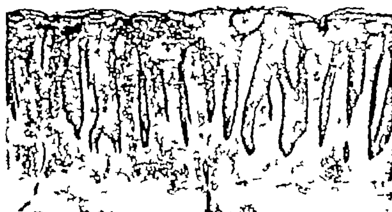


Fig. 141.—Chronic eczematous dermatitis irregular acanthosis, spongiosis, vesiculation and dermal inflammation. (Miller ADM 56 678 1947.)

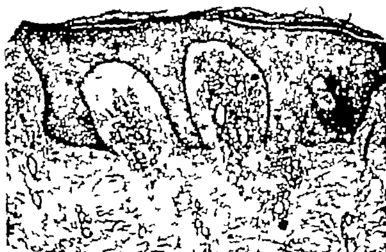


Fig. 142.—Chronic lichenified dermatitis of leg sclerosis, vasodilation, and acanthosis. (Dr. Fred Weidman.)

may become lichenified, especially if seborrheic dermatitis or medicinal irritation is superimposed *T purpureum* causes lichenoid lesions. Atopic dermatitis (p 484) is lichenoid, but atopic and circumscribed lichenification are not the same (Brunsting ADS 34 935 1936) a view with which Tachau (YBD 1939 p 83) would disagree Occipital lesions occurring almost exclusively in women are due in part to irritation from the hair brush, according to Molesworth (UCutRev 50 61 1946) Cases affecting the legs are often ascribed to venous incompetence (Heverdale and Cannon ADS 44 52, 1941) but this is not the whole story We feel that contactants, foci of infection perhaps food allergy and certainly locally precipitating agencies such as trauma, infection, and defective circulation are all concerned. Hemolytic *Staphylococcus aureus* is the only pathogen we regularly cultivate from typical leg and ankle lesions.

**Pathology**—Changes comprise hyperkeratosis and areas of parakeratosis, long narrow epidermal pegs, moderate edema of the dermal papillae and diffuse infiltrations with small mononuclear cells. Pigment is increased in the epidermal cells and the chromatophores of the dermis are increased in number Elastic and connective tissues show little abnormal change See Sachs et al (ADS 54 397 1946)

**Treatment** is not reliably satisfactory For a solitary stabilized lesion such as might be found on the proximal extensor surface of the forearm, a few weekly doses of 150 r x ray therapy are usually curative In occipital cases in women, similar x ray therapy interdiction of mechanical and chemical irritation and a scalp lotion for dandruff are usually effective One need not avoid temporary epilation In cases affecting the ankles, with or without ulceration, the elimination of focal infection is often indispensable Not only teeth, gums, tonsils, and genitourinary organs require consideration, but also tinea of the feet and nails. Circulatory insufficiency requires surgical consultation regarding the veins, and internal medical aid may be summoned to deal with anemia swollen ankles, and cardiac or other visceral problems which are pertinent Guy et al. (ADS 57 822, 1948) discussed nutritional aspects and cleaned up dirty mouths to improve mastication Measures aimed at improving liver function helped eczematous patients, especially those with the commonest form congestive or varicose eczema of the legs, stated Fichenlaub and Osbourn (ADS 57 171 1948)

Other efforts in the treatment of lichenoid dermatitis include topical application of 5 per cent crude coal tar ointment 10 per cent silver nitrate occlusive bandaging repeated peeling doses of ultraviolet light Castellani's paint etc One may apply 25 per cent potassium hydroxide scrape off the scales and dress the lesion with Ichthyol ointment Peck uses pure coal tar for a few days, alternating with zinc paste occasionally blistering a lesion with solid $CO_2$ Stokes (J 105 1007 1935) stressed psychologic aspects of treatment giving suggestions as to how the patient may be induced to slow down We like 1 per cent phenol in zinc oxide ointment or 1:5000 $KMnO_4$ compresses if the lesion is exudative, elimination of focal, circulatory and systemic factors, then x ray therapy in 125 to 150 r doses rather than smaller fractional doses, which do not do the work.

## EXUDATIVE DISCOID AND LICHENOID CHRONIC DERMATITIS

A dermatitis of unknown cause and sudden onset occurring principally in Jewish males of 30 to 50 years of age was described by Sulzberger and Garbe (ADS 36 1 193 ) The widespread eruption is often preceded by circumscribed dermatitis which

is readily irritated by efforts at treatment. Pruritus is a prominent feature, worse at night and with crises accompanied by chilliness and paresthesias. Sharply demarcated oval and discoid plaques of rapid variation in consistency and appearance are seen. They may be flat and scaly, elevated and edematous, or oozing and crusted. Vesicles are evanescent, but punctate oozing with vesiculation of histologic dimensions occurs. The stages of oozing, scaling, and involution are brief, but some plaques become lichenified. While no area is exempt, predilection is evinced for penile, scrotal, and extensor surfaces and the perimammillary, circumoral, abdominal, and scapular regions. X-ray therapy aggravated the symptoms (as it does those of dermatitis known to be caused by resinous fabric finishes) and the disease did not respond to arsenic or anything else the original authors tried. Laboratory studies reveal perhaps slight eosinophilia, and that is all. Sections show slight edema, capillary and arteriolar dilatation, perarteriolar infiltration with inflammatory cells, not with those of mycosis fungoides, irregular acanthosis, spongiosis and some intraepidermal vesiculation (Sachs and Kirsch: JIn D 8: 15, 1947). The patient of Couperus (ADS 54: 374, 1946) was worse in the winter. Coal tar ointment relieved a patient of Bernstein (ADS 41: 1183, 1940). Pascher (ADS 42: 322, 1940) thought subcutaneous sodium arsenate helpful in 5 cases. Contactants were believed causative by Cannon (ADS 36: 1269, 1937; 48: 669, 1943; 55: 273, 1947) and by Sharlit (ADS 45: 776, 1942). Prolonged hospitalization may be required.

## ERYTHEMA

**Symptomatic Erythema** may result from physical or chemical agencies acting on the skin, producing vasodilation and so redness, which disappears under diascopy. Systemic diseases of many varieties and other derangements of the general economy which may be labeled intoxications, for want of a better term, may also cause erythema. Allergy is perhaps the commonest factor, for foreign proteins, serums and medicines frequently give rise to roseolas. Local, asymmetric distribution speaks for a local instigation of the symptom, and symmetry and widespread distribution are features of erythemas of internal origin. Neurologic influences as varied as blushing, the dependent cyanosis of psychoneurosis, and vasodilation following sympathectomy may be mentioned. The erythema of contact dermatitis is pruritic while other erythemas are generally practically asymptomatic. The pathologic changes are usually completely reversible.

One may list as illustrative, without intent to be exhaustive, erythemas symptomatic of systemic diseases: rose spots, sparse and small, on the abdomen especially in typhoid fever; the roseola of early syphilis; rashes in diphtheria, gonorrhea, meningitis, rickettsiosis, infectious mononucleosis (where the transient rash may resemble German measles, wrote Contratto: AIM 73: 449, 1944, or is sometimes scarlatiniform, according to Halcrow et al.: BMJ 2: 443, 1943), streptococcic and staphylococcic infections, maculopapular and generalized in toxoplasmosis (Pinkerton and Henderson: J 116: 807, 1941). Avitaminotic states may exhibit erythema, pellagra for example, and rashes in diabetes mellitus are probably of this nature (Rudy and Hoffman: NEngJM 227: 893, 1942).

**Pretibial Fever** is a curious epidemic febrile disease of abrupt onset with myalgia, splenomegaly, bradycardia and leukopenia, in which the striking manifestation is an erythematous rash, solely or predominantly pretibial in distribution, appearing about the fourth day (Lipscomb and McMahon: J 128: 90, 1945).

**Erythema of the Palms** with diffuse or blotchy redness due to arteriolar dilatation is seen in portal cirrhosis ("liver palms"), chronic gastrointestinal and pulmonary disease, rheumatoid arthritis, malnutrition and pregnancy (Perera: J 119: 1417, 1942; Lofgren: ADS 46: 302, 1943; Ratnoff and Patek: Med 21: 207, 1943). Palmar erythema of a peculiar type affecting especially the volar eminences and without symptoms, was discussed by Walsh and Becker (ADS 44: 616, 1941) who called attention to its association with spider nevi and its onset during pregnancy in 4 of the 20 collected cases. See Bean (AmHJ 25: 463, 1943). Erythema palmare, p. 36; Telangiectasis, p. 590.

**Dukes Disease (Fourth Disease)** is a mild roseola exanthem occurring in children. Premonitory symptoms are slight, with or without sore throat. It is seen usually in the spring or summer months. The eruption is bright rosy red, and slightly

edematous but not hot to the touch. It may cover the body within a few hours. Lymph nodes become large and tender. Fever rarely reaches 104° F. Desquamation follows. There is no cross immunity with German measles.

**Erythema Infectiosum (Fifth Disease).**—This feebly infectious disease, characterized by its rash, but otherwise practically without symptoms, has been reported from scattered parts of the world. It occurs in epidemics, is a disease of early childhood, appears in the spring and summer and produces no cross immunity with other exanthemas. Determination of the cause has baffled every investigator. Kerr and Marsh (AmJPubH 23: 1271, 1933) reported an epidemic of 25 cases in 11 weeks at Elmsford, N. Y. The incubation period was 4 to 14 days. The epidemic in a New York orphanage described by Chargin et al. (ADS 47: 467, 1943) comprised 170 attacks in 80 patients among the 137 children. The eruption is maculopapular rose-red and more pronounced on the face, legs and arms. It appears first on the cheeks and may be limited to this location (Rector: JPed 15: 540, 1939). The lesions are peculiarly circular and crescentic. They enlarge peripherally, undergo confluence, heal in the central zone, and so produce a geographic, annular and angularly mottled appearance that is quite striking. The skin is swollen and warm, but does not itch. The patient's temperature may rise to 101°, rarely. Mild leucopenia may be found. There is no adenopathy or splenomegaly. The eruption disappears in about 4 days, leaving no scale, scar or pigmentation. No treatment is indicated.



Figs. 443 and 444.—Sixth disease (exanthem subitum). (Dr. L. H. Barenberg.)

**Exanthem Subitum (Roseola Infantum, Sixth Disease)** is a mild disease affecting principally children under 3 years of age. Most cases occur during the fall, with some in winter and summer. The incubation period seems to average about 10 days, but infectiousness is not great. The onset is acute with a temperature of from 102° to a high rarely over 103° F., accompanied by evidences of upper respiratory infection and tonsillar and pharyngeal congestion. The child is irritable but not toxic. In some of the patients of Barenberg and Greenspan (AmJDisChild 58: 983, 1939) fever was highest at first and fell by crisis, while in others the maximum was reached on the second day and fell gradually. The rash is rubelliform, affects the whole body, is discrete on the trunk and tends to be confluent about the neck. It appears at the time of fall of temperature about 4 days after the initial symptoms of illness. At this time there are lymphocytosis and usually mild leukopenia. Lymphadenopathy is not

present as a rule a distinction from rubella. Complications are extremely rare; the disease is relatively trivial; the rash f des in 2 days or so. Symptomatic treatment with aspirin, a barbiturate, and phenolated calamine lotion suffices. See Jennings (JMRoc¹J 37 677 1940) Jones (VaMMonth 66 401 1939) Greenthal (WiscMJ 40 .1, 1941)

# ACRODYNIA

**The Pink Disease,** Erythredema and Swift s Disease are synonyms of this rare disorder of infants. The onset is insidious with loss of weight anorexia and listlessness. The basic sympt ms comprise a profound hange in temperament muscular hypotonia and tachycardia, according to Fisher (BMJ 1 231, 1947): The hitherto thriving infant loses his normal contented disposition and gradually comes t present a picture of unhappiness far exceeding in intensity and duration the intermittent fractiousness f teething, t which process the symptoms of the disease are at first too readily ascribed. Unhappiness increases until he exhibits a continuous, miserable peevish resentfulness or an active, militant fury against all the agencies of the external world. Muscular hypotonia may be extreme Walking if attained is lost The infant droops spinelessly in the mother s arms with its face buried in her shoulder The thigh muscles especially lie flaccid and feel a if ecml fluid. The pulse ranges from 144 t 166 or even higher when the child is provoked. Cutaneous symptoms are variable. In classic cases, the hands and feet become swollen, painful and itchy cold and clammy and pink or dusky red. Perspiration is excessive and a pruritic sudaminal eruption criss-crossed with excoriations may be found on the trunk and limbs. The rash may be transient or may persist for weeks. Sweating gives the skin a moist cold flabby almost reptilian feel. Desquamation appears from ² to 3 weeks later and its inten t parallels that of the rash. Buccal and conjunctival irritation are manifested by refusal of food and photophobia with perhaps no external findings, or only mild evidences or quite troublesome inflammation. Secondary infection may cause ulcerative stomatitis, sloughing of gums, bronchopneumonia, which caused 7 of the 9 deaths in Fisher 63 cases.

**Etiology.**—The cause is not known, but neurologic infection, intoxication, and nutritional deficiency are suspected. There is no seasonal or racial predilection. The peak age of incidence is 9 months, and fewer cases are found after 12 months. Resemblance to ergot poisoning was noted by Debré and Kévot (abs J 112 1772, 1939) Warthin resembles that of encephalitis (Groom BMtMJ 35 616, 1941) slight meningeal irritation (APath 1: 64, 1926) found at autopsy extreme edema and slight meningeal irritation f the central nervous system, chronic erythema of the skin with hyperkeratosis, and the ges due to terminal respiratory infection or gastroenteritis to h m these abnormal lities recalled the changes in pellagra. See also Blackfan and McKhann (JPed 3 44 1933) Crawford (PaMJ 42 473 1940)

Treatment requires good n rsing good body hygiene patience in feeding, mild sedation and topical soothing (Fisher) A high  lanum rat be is generally urged but it was the addition f nicotinic  cid that seemed effecti e in the patient of Jahn and Dornberger (KebrBMJ 4 391 1939) Large amounts of $B_1$ and of wheat germ were recommended by Forsyth (MJAustral 2 731 1939; 1 78 1941) Injections f $B_1$ inadequately absorbed by mouth, appeared corat to Durand et al. (JPed 14 74 1939) The  fants reported by Elmore (Ped 1 643, 1949) and by Bi ings and Lewis (JPed 32: 63, 1948) had received calomel prior to the onset f the pink disease, nd they responded favorabl t BAL. It seems possible that mercurial intolerance explains the condition.

# ERYTHEMA MULTIFORME

**Symptoms.**—Erythema multiforme is an acute inflammatory disease characterized by the devel pment of reddish macules, papules and vesicles with symmetric distribution The lesions vary greatly in size and configuration and papular nodular vesicular circinate marginate and iris clinical forms are recognized Erythemato-papular types may be separated descriptively from the vesico-bullous ones (Keil AnnIntM 14 449 1940)

The sites of predilection are the sides of neck and face dorsal surfaces of hands and forearms, l gs, dorsal surfaces of feet and mucous membranes. The lesions are bright or dark red in color fading to a purplish or violaceous hue Symptoms are slight as a rule. An attack seldom lasts

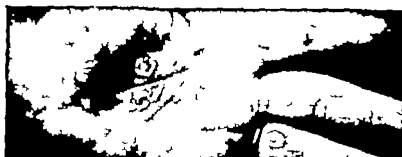


Fig. 645.—Erythema multiforme: iris-like lesions of palm.



Fig. 646.—Erythema multiforme.



Fig. 647.



Fig. 648.

Fig. 647.—Erythema multiforme.

Fig. 648.—Eruptive fever with stomatitis and ophthalmia. (Glanzmann: AmJDisChild 40: 1148, 1930.)

longer than 2 or 3 weeks. The lesions develop quickly and the inflammatory process may be of sufficient intensity to convert papules into vesicles with serous or even bloody contents. On the absorption of effusion iris-like lesions are formed, and these continuing to enlarge, may coalesce with neighboring rings. Mucosae are often involved, otological changes being sometimes of such prominence as to obscure recognition of skin changes (Howard and Wible AnnOtol 55 146 1946) Ocular complication is sometimes seen, with catarrhal or purulent conjunctivitis sometimes causing corneal ulceration (Koke AOphth 25 78, 1941) In all types the color entirely disappears on pressure. Scarring is infrequent but can result from secondary infection

**Etiology.**—Numerous theories have been advanced to account for its causation. The cases of Osler (BJD 12 227 1900) manifested urticaria, angioneurotic edema purpura exudative erythema, leucocytosis, splenomegaly fever arthritis, colic, vomiting melena, asthma and emphysema, alone or in combination Similar cases have more recently been recognized as allergic in nature (Stokes MCNAm 8 875 1924) Perhaps specific micro-organisms are concerned, but findings are not uniform (Guy J 71 1993 1918) The disease occurs oftenest in the fall and spring A relationship to herpes simplex was discussed by Anderson (ADS 51 10 1945) The similarities of erythema multiforme and erythema nodosum interested Noojin and Callaway (ADS 54 560 1946) who stressed the coexistence of focal infection in both conditions. An accompanying pneumonitis without demonstrable parasitic cause was observed in the predominantly mucosal cases of Dingle et al. (AIntM 78 687 1947) Cases with high, intermittent and prolonged fever occur and despite articular pains and a duration even of months the prognosis is favorable (Leopold AmJDisChild 59 1298 1940)

**Pathology.**—Changes in the cutis are those of acute, localized inflammation. In the papillary layer are vascular dilation, perivascular cellular infiltration and proliferation more or less emigration of leucocytes and even of red cells, and edema. Collagenous tissue is swollen and transparent.

**Diagnosis.**—The multiformity the bright or dark red color of the eruption, its symmetric distribution and predilection for the dorsal surfaces of the hands and feet and the sides of the neck, the tendency to assume ring shapes, and the absence of itching are characteristic The disease may be confused with urticaria, which it occasionally resembles, but the rosy color and limited distribution of the lesions and their nonpruritic character together with the fact that they are never as transitory as those of urticaria should prevent error Bullous cases are distinguished from pemphigus by their multiform character color and distribution

**Treatment.**—Rest in bed is desirable Foci of infection should be sought out and eradicated. Various internal remedies, such as quinine salicin, potassium iodide and ergot have been recommended, but are of dubious value Sodium salicylate in large doses may help Sulfanilamide has been curative in some cases. Small doses of Benadryl promptly relieved 2 patients of Pinkus (AnnAllergy 4 288 1946) Locally powders, calamine lotion, or aluminum acetate packs are indicated

**Bullous, Malignant Erythema Multiforme (Eruptive Fever With Stomatitis and Ophthalmia Ectodermosis Erosiva Pluriorificialis Dermatostomatitis).**—A striking picture is seen in such cases as were described by Ginandes (AmJDisChild 49 1148, 1935) Young persons, especially males, are the usual victims, more commonly

during the spring season. The onset is abrupt with a temperature of 102° to 104° F, headache, chill, malaise, sore mouth and throat, and frequently the symptoms of upper respiratory tract infection (Soll: ArchIntM 79: 47, 1947). Vesicles appear on the lips, tongue and buccal mucosa; they become pseudomembranous lesions, with or without ulceration. Salivation is profuse. Conjunctivitis, rhinitis, balanitis and sometimes anal involvement of variable intensity accompany the oral and constitutional symptoms. Within a few days, erythematous macules, vesicles and petechial lesions appear on the hands and feet and to a less degree elsewhere on the body. The exudative lesions



Fig. 649.—Eruptive fever with stomatitis. (Dr. C. C. Dennie.)



Fig. 650.—Erythema annulare centrifugum. (Hopkins, AD&S 40: 14–, 1939.)

crust and heal in a period of 3 to 6 weeks. In 9 cases reported by 1935 only 8 were not totally blinded by the effects of the disease.

The course, consisting of sudden onset, rapid rise to maximum intensity and gradual return to normal, suggests a violent, transient virus infection as the cause. Granados' patient presented dark, red oval elements many of which developed necrotic centers, and persistent brown stains marked the sites of disappearance of inflammation; the blood culture was sterile, as is usual. Severe symptoms persists for little more than 10 days. Costello (JInvD 8: 137 1947) reported 33 cases, 17 in detail, with 9 deaths and necropsy an upper respiratory onset occurred in more than half of his patients, and he suspected a virus cause. See Reiter and Behcet's syndromes, p. 169

Four cases were reported and the literature reviewed by Klauder (ADS 36 1067 1937) who placed the syndrome with erythema multiforme and emphasized the variability of that disease. Lever (ADS 49: 4 1944) stressed the features of severity and eye damage despite the rarity of fatality. Pneumonitis seems to be a part of the picture (Silver AnnIntM 41: 499 1946). Stanyon and Warner (CanadMAJ 53: 427 1945) describing this mucosal respiratory syndrome, noted its gradual onset of 4 to 14 days, followed by suddenly severe symptoms, during which sulfonamides and penicillin were without value; they suspected a virus cause.

The patients of Walton (Lancet 2: 314, 1941) were relieved of chest symptoms but not of mucosal ones by sulfonamides, and transfusions seemed especially beneficial. Robinson (ADS 52: 91, 1945) attributed the sharp crisis in his patient to penicillin after sulfonamides had done no good. Cultures made from the eyes reveal *Staph. aureus* as a rule, often accompanied by streptococci, observed Goldfarb (JPed 28 679 1946) and vision has been preserved, he stated, only in patients who received adequate antibacterial chemotherapy. Sulfonamides and penicillin prevented permanent eye damage in the cases of Wright et al. (AIntM 79: 510 1947). Benadryl appeared to relieve the patient of Schoenperlen (CanadMAJ 56 72, 1947).

**Erythema Annulare Centrifugum** is an erythema multiforme-like disease characterized by a centrifugally progressive annular erythematous eruption. The eruption begins with discrete papules, which enlarge so that within a few hours circular red areas are present. The thickened, firm, pinkish border may be elevated and even somewhat scaly. Evolution and confluence of lesions result in the production of festooned, arcuate or polycyclic figures, which tend to clear centrally and to become concentrically banded. They may cover large areas of the trunk, rarely involving the face. Their appearance changes quite rapidly: a design breaks up, disappears, and is replaced with new elements of the same type. Symptoms are mild and variable but generally do not exceed moderate itching. The eruption tends to involute of itself, reappear rapidly and again disappear and so is manifested as a chronic relapsing disease. We have seen cases associated with vesicular tinea of the feet. We believe that the disease is sometimes a dermatophytid. Compare Erythema Gyratum Perstans.

**Erythema Gyratum Perstans.**—A chronic type of erythema which was characterized by the occurrence of persistent erythematous patches, which assume annular, marginate, and gyrate forms, differing essentially from other varieties of erythema, was reviewed by Wende (J 51 1936 1008). The trunk is the site of predilection for the development of the lesions which usually are at first red in color but later assume a purplish or violaceous hue. They finally disappear leaving a brownish, pigmented patch, which may be uniform, but often is stippled or reticulated. Klaber (BJD 58 111, 1946) reviewed the presumably distinctive features of marked pruritus, wide extension of the disease, prolonged duration, onset in early years, familial incidence, the vesicular border and collarette desquamation, but no feature seemed entirely reliable diagnostically. Typical cases are rare, and differentiation from erythema annulare centrifugum is dubious. Erythema chronicum migrans is probably the same disease. A relationship with dermatitis herpetiformis is hypothesized.

## ERYTHEMA NODOSUM

**Symptoms.**—This inflammatory dermatosis is characterized by an eruption consisting of a few or several rounded or oval, painful nodules which persist for 2 or 3 weeks and then disappear spontaneously. The nodules reach their full size rapidly. They may be firm or elastic, or soft in consistency and are deeply embedded in the skin. They are oval, tense, shiny and bright red in color and commonly involve the extensor surfaces of the arms and legs, particularly the anterior tibial regions.

In diameter they range from 1 to 5 cm., and are often raised slightly above the surface of the surrounding skin. Their outline is fairly well defined but not sharp They are painful and tender They gradually subside, changing in color from bright red to red, then dark red and purplish, and finally disappear leaving greenish or brownish stains, which persist for a few weeks. Suppuration of the nodes occasionally occurs but is a rare complication. In number the lesions range from 2 or 4 to 20 or more They are generally symmetric. Nodules may appear in crops and the attack may be prolonged over several weeks (Klauder ADS 36 1067 1937)

**Etiology**—The disease occurs most frequently between the first and third decades, and during the spring and fall. The lesions can be caused by several different agencies drugs, such as iodides, bromides, sulfonamides, and antipyrine tuberculous, coccidioidal and streptococcic infection and miscellaneous diseases including syphilis, leprosy filariasis, lymphopathia venereum, erythema multiforme, trichophytosis, chancroid, influenza, ulcerative colitis, rheumatic heart disease (Spink AIntM 59 65 1937 Poppel and Melamed NEngJM 227 325 1942) Excepting the regions where coccidioidal disease is endemic, tuberculosis is a common cause. Erythema nodosum may be thought of as a nonspecific allergic syndrome (Edit. J 112 147 1939) A known respiratory infection antedated erythema nodosum in 126 of 155 cases studied by Favour and Sosman (AIntM 80 435 1947) Half of their throat cultures revealed beta hemolytic streptococci migratory polyarthritis was part of the picture in four fifths of the adults and in one third of the children but rheumatic heart disease was a rare sequel



Fig 112.—Erythema nodosum, typically affecting shins.

**Pathology**—The epidermis is little altered. The vessels of the papillary plexus are dilated, with extravasation of both white and red cells. In some capillaries, leucocytes are packed so closely as to resemble white thrombi There is widespread infiltration throughout the corium. Late in the disease, disintegration of extravasated red cells gives rise to more or less pigmentation.

**Diagnosis**—The multiplicity of the lesions, their symmetry their tenderness, and the attendant constitutional symptoms, should serve to differentiate them from gummas, bruises, and staphylococcic abscesses. From the abscesses of sporotrichosis they are to be recognized by their bilateral distribution and the absence of a chancre. In erythema induratum the sites of predilection are the calves, the disease is of slow development, the lesions are dark red from the beginning and sometimes ulcerate, and the histologic structure is that of tuberculosis.

**Heberden s Nodes** are tender firm bony outgrowths of insidious onset in persons of middle age at the sides of the distal interphalangeal joints of the fingers in primary osteoarthritis (J 119: 83., 194 ) The toes are not similarly affected. They are 10 times as common in women as in men (Stecher and Hauser AmJR 59: 326, 1948)

**Osler s Nodes** are reddish swellings, pea to almond size with whitish centers, lasting only a day or so located in the pads of the fingers and toes, the thenar and hypothenar eminences the sides of the fingers and skin of the forearm. These were seen in of 10 of Osler patients with chronic bacterial endocarditis.

**Erythema Elevatum Diutinum** was the name applied to a persistent nodular eruption, occurring chiefly in young women by Crocker and Williams (BJD 6: 1, 1894) Similar symmetric, purplish, congestive lesions were seen also in elderly gouty men. The lesions appeared to be inflammatory fibroses analogous to subcutaneous rheumatic nodules Analyzing previous reports, Ketron (ADS 50 363, 1944) illustrated a rheumatic woman whose photographs are reminiscent of eruptive xanthoma affecting buttocks, extensor region of elbows and dorsa of hands, but fat was not found in sections of the irregular reddish or purplish plaques, elements of which sometimes healed spontaneously w thout scar Ketron described a toxic hyalin about the blood vessels. The patient of Weidman and Besancon (ADS 20: 593, 1929) was also rheumatic. The possible relationship to granuloma annulare wa discussed by Templeton (BJD 40: 193 1928) but denied by Combes et al. (ADS 5 19 1945)

## PERIARTERITIS NODOSA

Periarteritis nodosa was first described by Kussmaul and Maier in 1866 as a rare and generally fatal disease characterized by local inflammation of arteries arterioles, with thrombosis, aneurysm, o hemorrhage and circumscribed necrotizing and exudat arteritis Mesarterit occurs, with necrosis f part of the media, polymorphonuclear infiltration and extens on f the process. Males have been affected four times a often as females. The organs i l ed ha e been the kidney in 80 per cent f the cases, the heart in 0 per cent the liver in 65 per cent, the mesentery in 30 per cent the muscles in 30 per cent the pancreas in 25 per cent the central nervous system in 8 per cent. The lesions may be of cute subacute and chronic forms and may heal lesions in several stages may coexist

Symptoms depend on the organs affected and are characterized by acute or gradual onset, muscle and joint pains, fever abdominal pain edema, weakness, paresthesia, diarrhea, insomnia, billiness, sweating purpura, angina, progressive weakness, emaciation, and jaundice Death results f there occurs intolerable damage to vital structures, such a renal insufficiency cardiac failure rupture f an aneurysm. Subcutaneous nodules occur in 20 per cent They are pea to hazelnut-sized, freely movable on the subcutaneous tissues fixed abov t the skin as a rule They are evanescent. Petechiae appear in 15 per cent Alkiewicz (AfDuS 168 322, 1933) assembled the findings in 36 ases w th ki involvement there were present macules in 16, nodules n 15 nodes in 11 petechiae n 7 and necrosis 5. The lesions do not commonly break down. The nodules may be pulsat le

A f irly typical eruption occurs in the chronic and more benign form of periarteriti nodosa. Li id brown, macula and infiltrated lesions are found especially upon the lower extrem ties, accompanied by joint pain and papular urticaria, and in some cases by racemose l id t of a member

Probably not a rare as once thought some 400 cases of the disease have been described (Edit J 133 621 1947) It ppears to represent n allergic reaction f the small arteries t arget f antigens, for haracteristic vascular lesions ha e been found in patient who died following hypersensitive reactions to therapeutic sera and have been produced in rabb t by est blishing a cond t on analogous to serum sickness (Rich and Gregory BullJHH 72 65 1943) Trichinosis wa apparently the cause in cases of Reumann (J 122 ?4 1943)

Typical circumscribed inflammation f the skin arterioles is found on microscopic examinat on f the les on Hemorrhage accounts for the brown stain. There are 4 stages in the pathologic processes (1) necrosis f the innermost part of the media of small arteries or of th outer part of the media f arteries which possess vasa vasorum; (2) followed by flammation w th exudation of eosinophiles, lymphocytes, plasma cell and pol morphonuclears, later by prol feration of fixed tissue elements about the vessels, and perhaps the beginnings of aneurysms or nodes, the proliferation of the intima leading t infarction (3 the hronic st ge w th granulation tissue and heali g with scar; (4) finally th healed st which rarely seen.

Treatment is largely symptomatic, main reliance being placed upon rest and eradication of foci of infection. Arsphenamine has been used.

**Arteritis of the Temporal Vessels.**—A group of cases of arteritis limited to the temporal vessels has been observed by Horton et al. (J 106 46 1936). These are characterized by their nonfatal nature, by their attack upon elderly persons, by the severely painful, circumscribed reddish, tender nodules in tortuous and enlarged temporal arteries, and by the accompanying headache, malaise, lassitude, weakness, fever, night sweat, anorexia, loss of weight, anemia, and difficulty in hearing. The condition endures for 4 to 6 months. There is some therapeutic response to large doses of potassium iodide. Excision of the artery is the most effectual procedure. No cause has been determined. The disease had not been found in a patient younger than 53 years of age. Dantes (J 131 1265 1946) noted that women are affected twice as frequently as men. The disease is remarkably localized, though retinal and oral involvement have been identified. Histologically a multinucleated giant cell inflammation in focal distribution is the interesting feature (Edit. J 131: 669 1946). Temporary relief was obtained in 4 cases by periarterial injections of procaine by Roberts and Askey (J 137: 69 1948).

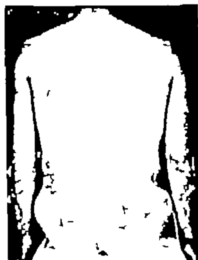


Fig. 4 4



Fig. 455.

Fig. 454.—Periarteritis nodosa, showing ... (Ketron and Bernstein, Arch. ... 40 929, 1939.)

Fig. 455.—Periarteritis nodosa, inflammation of vessel. (Drs. Ketron and Bernstein.)

## GRANULOMA ANNULARE

**Symptoms.**—Granuloma annulare is a chronic inflammatory dermatosis characterized by grayish white or pinkish, flat topped, intracutaneous nodules which spread centrifugally and form circular and arcuate lesions. The disorder usually develops slowly, the first clinical manifestation being a localized, deep-seated infiltration of the skin without appreciable reddening. Ringlike lesions result from central involution and peripheral extension. An annular lesion is often beaded. Mature lesions are slightly raised and of a firm or doughy consistency. The sites of predilection are the backs of the hands. Wrists, feet, ankles, neck, knees, and buttocks may be affected. Lesions are usually, but not always, few in number and range from 0.5 to 5.0 cm in diameter. On superficial examination the central portion of the rings appears normal, but atrophic changes may often be noted. Subcutaneous lesions do occur rarely.

**Etiology.**—The cause is unknown. It is a comparatively rare disorder. It occurs most frequently in children, and develops oftenest during the summer months. Michael (ADS 29: 189 1934) with a report of 8 cases, concluded that there is no evidence favoring the hypothesis of tuberculous origin.

**Pathology.**—*In the subpapillary region there is widespread* cellular infiltration with lymphocytes, polynuclears, epithelioid cells, and spindle cells of the connective tissue type. In old lesions necrosis occurs in the center of the infiltrated areas. While similarity to necrobiosis lipoidica was noted by Ellis (ADS 43: 822, 1941) Combes and Bluefarb (ib 42: 441 1940) and Laymon (TransADA 1947) distinguished the disease clearly from erythema elevatum diutinum and necrobiosis. Mucin was found mainly in foci of altered connective tissue in 24 of 29 cases by Freudenthal (BJD 57: 177 1945) confirming the observations of Pruntv and Montgomery (ADS 46: 394 1942).


Fig. 656.


Fig. 657.

Fig. 656.—Granuloma annulare
Fig. 657.—Granuloma annulare, histology. (Dr. Stuart Way.)

**Prognosis.**—The disorder is essentially benign, though chronic. The lesions may persist for months or years, and then disappear spontaneously. The nodules never ulcerate.

**Treatment.**—Roentgen therapy is efficient, although lesions are liable to recur. Freezing with solid carbon dioxide will generally cause a nodule to disappear. Spontaneous regression after biopsy has been seen, and sulfonamides and penicillin have apparently cured some cases but are not dependable therapeutic agents. O'Farrell (ADS 50: 323, 1944) saw 2 cases clear after intercurrent measles.

## PITYRIASIS ROSEA

**Symptoms.**—Pityriasis rosea is an acute inflammatory dermatosis characterized by a self limited eruption of numerous, yellowish, pinkish, or reddish, scaly macules of various sizes and shapes, asymmetrically distributed over the trunk and limbs. As a rule constitutional symptoms are entirely wanting. An initial large, single plaque, likely to be somewhere

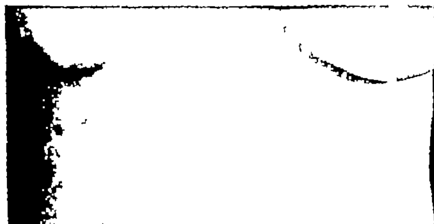


Fig. 438.—Pityriasis rosea, herald patch on epigastrium. (Dr Clyde Cummer)

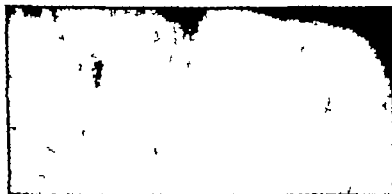


Fig. 439.—Pityriasis rosea, early lesions.



Fig. 440.—Pityriasis rosea.

on the trunk, usually precedes the general outbreak by 1 or 2 weeks. The lesions develop as oval macules of irregular outline or slightly edematous maculopapules, from 0.5 to 5 cm. in diameter thinly covered with soft white thin, branny scales. The long axis of a lesion parallels the lines of cleavage of the skin. The border is somewhat irregular and is not definitively sharp. The patches may increase slightly in size, and the central portions tend to clear, giving rise to slightly elevated reddish rings with fawn-colored centers. *The eruption may be limited to the trunk, but the* upper arms and the thighs frequently are attacked. Rarely is the face involved. Symptoms are mild although itching may be present, especially when the patient perspires, and in severe cases. The eruption disappears spontaneously in from 6 to 10 weeks. Recurrences are rare but are recognized at times. The duration of an attack seldom exceeds 2 months (Niles and Klump. ADS 41: 265, 1940).

Unusual and anomalous varieties are common. They were classed by Klauder (J 82: 178, 1924) in macular, urticarial, papular and vesicular forms. Oral involvement occurs occasionally in the form of ruffled desquamation or tiny erosions (Gucquierre and Wright, ADS 43: 1000, 1941), and when fever accompanies the disease oral lesions are likely to be found (Costello, ADS 53: 73, 1946). Axillary vesiculation generally is present in extremely severe cases.

**Etiology.**—The cause is unknown. If the disease is infectious, it is feebly so. The disorder appears to be due to some sort of parasitism despite the absence of a demonstrated specific agent. The onset often coincides with the wearing of a new garment (Epstein, UCutRev 47: 61, 1943).

The age incidence is highest between 10 and 30 years. The seasonal incidence is highest in the fall and spring months. The location of the primary plaque occurred on the anterior thoracic wall in 30.1 per cent of the extended series of cases of Niles and Klump. See Percival (BJD 44: 241, 1932).

**Pathology.**—The papillary vessels are dilated, and there is abundant cellular infiltration consisting of many lymphocytes and a few plasma cells and mast cells. There are numerous minute vesicles in the upper regions of the epidermis, and parakeratosis is seen.

**Diagnosis.**—The disorder is to be differentiated from seborrheic dermatitis, tinea corporis, squamous and circinate secondary syphilids, and acute psoriasis.

Seborrheic dermatitis develops more slowly, the scales are greasy, and the sternal and axillary regions seldom escape. Tinea corporis usually begins on some exposed part; the lesions are seldom numerous, they develop slowly, and fungi are demonstrable. Papulosquamous and circinate syphilids are infiltrated, give rise to pigmentation and atrophy, and frequently involve the palms; concomitant signs of syphilis, including a positive serum reaction, are present. In psoriasis the infiltration and scaling are more marked, the elbows and knees seldom escape, bleeding points are to be found, and the disease persists.

**Treatment.**—The eruption will disappear spontaneously within a few weeks. A mild parasiticide is possibly beneficial, and an antipruritic agent may be combined with it.

| | | |
|---|---|---|
| ℞ | Phenol | 0.3 |
| | Zinc oxide ointment | |
| | Ammoniated mercury ointment 3% | āā 8.0 |
| | Lanolin | 10.0 |
| | Lime liniment | to 30.0 |

Sig.: Apply for relief of itching.

A few erythema doses of cold quartz irradiation are likely to be curative. Sulfur preparations are irritating and valueless. Cool baths in 1:15 000 $HgCl_2$, with suitable precautions, may be used successfully (SMJ 35 597 1942). A single intramuscular injection of typhoid vaccine is recommended by Ebert and Otsuka (J 123 1036 1943). Vass (ADS 51 203 1945) obtained cures by the use of trichophytin 1:500 intradermally starch baths, and loose clothing to the latter rather than to specific effects of the antigen. Carpenter (ADS 52 184 1945) attributed her results.

## LICHEN PLANUS

**Symptoms.**—Lichen planus is an inflammatory dermatosis characterized by an eruption of small glistening violaceous papules which are discrete but may coalesce to form rough scaly patches. The disease may be acute subacute or chronic. In the acute form the outbreak, which is sudden, is accompanied by some malaise. The eruption may be general but is usually limited to certain regions. The papules are small and flat, with plane or slightly indented tops and angular bases. The surface of the papule may be marked by striae or grayish puncta, Wickham s striae, and the lesion is often capped by a thin scale. In color the papules range from bright red to violaceous, and as a rule, but not always, they are intensely itchy. A line of papules along a scratch is frequently seen. The acute form may merge into the chronic or an acute attack may supervene on the chronic. In the chronic type, the disease usually begins insidiously. The sites of predilection are the flexural surfaces of the wrists and forearms, the inner aspects of the knees and thighs, and the region of the lumbar spine. The face and scalp generally escape. The eruption is symmetric as a rule. On departing the lesions are likely to leave temporarily pigmented spots, sometimes slightly atrophic scars, particularly if they have been of long standing.

Lesions of the mucosae sometimes develop days or weeks before the integument is involved. On the buccal mucosa and on the tongue the eruption occurs as sharply defined, whitish patches or streaks, and on the glans penis it may take the same form although the papules may be of the cutaneous sort in size and contour. Occasionally the mucous membranes alone are involved. Vulvar lesions are not different from those of mouth or lips. Lichen planus affects other mucosae occurring even in the bladder (Young JUrol 43 265 1940). Leucoplakia of neoplastic nature and lichen planus, whitish and soggy where it is continually moist are different conditions. Nail involvement may be manifest as longitudinal striation grooves, tumefaction of the matrix, or psoriasiform pitting it is not pathognomonic (Lewis and Riechruth ADS 42 607 1940). Volar involvement particularly of the soles, may become extreme. Purplish tint and absence of vesicles are features distinguishing lichen planus from tinea.

Lichen planus is generally a persistent disease lasting 3 months or so, and it tends to recur even after apparent cure sometimes 10 years later.

Annular linear and rarely vesicular lesions occur as aberrant types of lesions. Linear lichen planus resembles a linear nevus unius lateralis its curious distribution is unexplained (Senear and Caro ADS 43: 116 1941). Lichen sclerosus is different an entity in which the lesions are atrophic and morphea like (Montgomery and Hill ADS 42 755 1940). Related atrophic lesions, including atrophic lichen planus, were studied by Wise and Rosen (JCutDis 35 66 1917). Some cases of lichen spinulosus

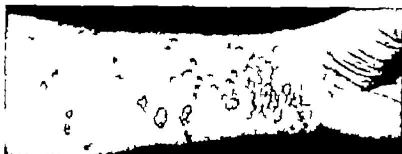


Fig. 661.—Lichen pla us, typical location. Note angularity of olaceous papules.

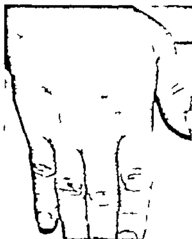


Fig. 662.



Fig. 663.

Fig. 66_.—Lichen planos.
Fig. 663.—Lichen planes annular lesion of flexure of wrist.

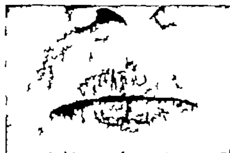


Fig. 664.



Fig. 665.

Fig. 664.—Lichen planus f lips.
Fig. 665.—Lichen planus of buccal mucosa.

Fig [illegible] —Generalized lichen planus (Drs Fordyce and MacKee)

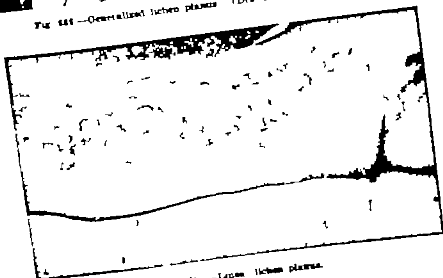


Fig [illegible] —Linear lichen planus.

are in fact an acuminate and atrophic form of lichen planus (Ellis and Kirby-Smith ADS 43 628 1941) This occasions alopecia which lacks the follicular plugs of folliculitis decalvans (Sachs and DeOreo ADS 45 1081, 1942) A follicular circumscribed form exists, affecting parts other than the scalp (Combes and Bluefarb ADS 44 46, 1941)

**Etiology**—The cause is unknown. Nervous exhaustion is thought to be an important contributory factor [avitaminosis?] The disease occurs especially during adulthood. The disease probably is a systemic one with cutaneous lesions. Focal infections, especially of the mouth and of genito-urinary organs, play an important part in the causation (Chipman J 71 1276 1918) Lichen planus developing after arsphenamine therapy was reviewed by Goodman and Sullivan (SMJ 36 401 1943) It is comparable with quinacrine lichen planus. The familial incidence of lichen planus was noted and discussed by Saffron (ADS 42 653 1940)

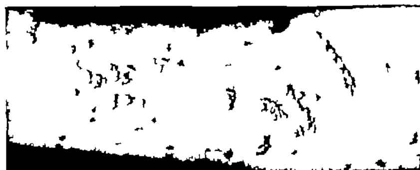


Fig 444.—Lichen pl nus, eruption in excoriations



Fig 445.—Lichen planus, histologic structure

**Pathology**—*Lichen planus papules possess typical* structural characteristics The horny layer is thickened and condensed and there is slight acanthosis, with stretching of the prickle cells. The papillae are enlarged, and the intrapapillary vessels dilated. There is a dense, sharply defined, cellular infiltration in the papillary and subpapillary layers. Lymphocytes predominate, with a number of polymorphonuclear cells, especially in newer lesions. The line of demarcation between dermis and epidermis is rendered indistinct by the dense, superficial infiltrate.

**Diagnosis.**—The disease is to be differentiated from psoriasis, lichen ified dermatitis, and papular syphilids. Oral lesions of lichen planus d

not fluoresce in Wood's light while those of neoplastic leukoplakia do (Costello NYSJM 46: 1778 1946) See Laymon (MinnM 25 863 1942)

In psoriasis the papules are scaly from the beginning and the scales are thicker and more abundant. Psoriatic lesions enlarge by peripheral extension; patches of lichen planus are formed by coalescence. In psoriasis the knees and elbows seldom escape involvement; there are minute hemorrhagic points when the scales are forcibly removed; and itching is inconspicuous. In contact dermatitis there is excoriation or lichenification, and the borders are not sharply demarcated. Lichen planus is a dry disease throughout its course. The miliary papular syphilid sometimes resembles papular lichen planus, but the color distribution, absence of itching, concomitant lymph node involvement and presence of a positive serum reaction render diagnosis clear.

**Prognosis.**—Lichen planus is an exceedingly chronic disease but one in which the results of treatment are usually gratifying.

**Treatment.**—The patient is to have the benefit of good plain food, hygienic living and, when possible, freedom from worry or care. Mercury is efficient. It is best given into the gluteal muscles.

℞ Mercuric salicylate ... 2.0
Lanolin ... 4.0
Oil q.s. ad ... 30.0
Sig.: Mercury salicylate in oil 1.0 c.c. equals 1 grain dose. Shake and inject aseptically 1 c.c. into the gluteal muscles every 3 days, if tolerated.

Bismuth is perhaps as effective as mercury. Acetarsone is often effective given in tablets of 0.25 gm. the maximum dose being 2 at a time 3 times a day for 4 days of each week for 6 weeks. It often provokes intestinal cramps, and its use entails all the dangers of the arsenicals. Bismuth arsphenamine sulfonate 0.1 gm. intramuscularly was advocated by Conrad et al. (SMJ 33 721 1940). Vitamin B complex by injection is a useful adjuvant (Burgess CanadMAJ 44 120 1941). Vitamin C, 100 mg daily may be given intravenously. Roentgen therapy in fractional doses abets systemic efforts. Given over the spine x-ray therapy was recommended by Driver (ADS 20 201 1929) but Hellier (BJD 55 11 1943) considered this no more effective than mercurial injections. Thiamin, 100 mg t.i.d. sometimes seems beneficial.

For local treatment an ointment may be prescribed as follows:

℞ Phenol ... 0.3
Ammoniated mercury ointment 5 per cent ... 12.0
Zinc oxide
Starch ... of each 4.0
Petrolatum ... 30.0
Sig.: Two per cent ammoniated mercury paste. Apply several times daily.

A soothing nongreasy application which the patient may apply at will is phenolated calamine lotion to which may be added from 1 to 3 per cent alcoholic solution of coal tar. Castellani's paint has some utility for coalescent patches.

It is essential that foci of infection be eradicated. We routinely examine the teeth by x-ray and order removed all dead and abscessed ones. We request treatment of pyorrhea when it exists and investigate the pelvis, cervix uteri or prostate.

**Quinacrine (Atabrine) Lichen Planus (Atypical Lichen Planus of the South-west Pacific).**—World War II brought forth numerous cases of peculiar dermatosis,

The patients were military personnel who had been on quinacrine for suppression of malaria for 3 months or more usually on K or C rations in a tropical climate and who had lost from 10 to 50 pounds in body weight (Bereston: JInvD 7 69 1946) New Guinea cases usually started on the dorsa of the feet as an indurated erythema suggesting contact dermatitis or pellagra. After a time an abrupt change would occur with exudation and dissemination similar to infectious eczematoid dermatitis, widespread involvement, including the scalp, where temporary alopecia was typical, and lymphadenitis as in exfoliative dermatitis. Lesions similar to hypertrophic lichen planus evolved, affecting by preference the flexor aspect of the forearms, inner thigh regions buttocks, and dorsa of hands and feet. These phases, well described by Goldberg (J 130 773, 1946) were not always separated chronologically Dry cases quite like severe lichen



Fig. 670 —Lichen planus-like eruption attributed to quinacrine, Southwest Pacific patient

Figs. 671 and 672 —Lichen planus-like disease attributed to quinacrine, Italian Theater patient.

planus occurred. Volar involvement was often marked (Barker ADS 55: 250 1947) Depigmentation and sometimes atrophic scarring were seen. Italian cases were recognized by Peterkin and Hair (BJD 58: 263 1946) Rectal lesions were seen by Warin et al. (BJD 60 249 1948)

The exact etiologic mechanism was never clarified, although quinacrine played seemingly an essential role. A husband and wife who changed their antimalarial from quinine to quinacrine developed this condition, reported Mitchell (ADS 51 353, 1945) Positive patch tests were reported by Duemling (ADS 52: 80, 1945) Flares following readministration of quinacrine were inconstant, Bagby (ADS 52: 1 1945) observing none and Bazemore et al. (ADS 54 308, 1946) reporting provocation in about 20 per cent. Since pure dermatitis medicamentosa may be expected to flare in 100 per cent of cases on readministration of the causative drug the way in which quinacrine caused this disease must have been other than by ordinary idiosyncrasy (Schmitt et al. ADS 52: 226, 1945) Blood quinacrine concentration diminished parallel with itching after cessation of the drug (Bigham: BJD 58: 71, 1946) In treatment, removal to temperate climate, penicillin, yeast, vitamin B complex, and elimination of quinacrine were effective measures, and pigmentary abnormality proved temporary See also Epstein (BullUSAMD 4 687 1945); Livingood et al. (J 129 1091, 1945); Nisbet (ADS 52: 221, 1945) Becker (ib 54: 335, 1946) Wilson (ib 54 377, 1946), Pillsbury and Livingood (ib 55: 441, 1947) Alden and Frank (ib 56 13 194 ) Nisbet (J 134 446, 194 ) Mitchell (ADS 57 436, 1948)

## LICHEN NITIDUS

Lichen nitidus is a rare, chronic, inflammatory dermatosis manifested by lesions which are characteristically firm, flat topped, shiny pinhead-sized, pinkish or flesh colored papules, which never coalesce or give rise to symptoms. The favorite site of involvement is the genital region, and the abdomen breast, and arms are sometimes attacked. Individual papules bear striking resemblance to those of lichen planus, but their color distribution, and absence of itching are distinctive

There are 2 varieties of the disease, wrote Niles (ADS 22 687 1930) (1) one showing a histologic resemblance to tubercle formation, and having an apparent relationship to tuberculosis elsewhere in the body and (2) one which clinically exhibits no etiologic relationship with tuberculosis and which shows the histologic picture of nontuberculous, inflammatory granuloma. The association of lichen nitidus with lichen planus is being more frequently reported, according to Ellis and Hill (ADS 33: 560 1936) who adding 2 such combined cases, recited the similarities of the two diseases.

The lesions are persistent and may remain for years without change. The rash was severe, confluent on the trunk, and cleared only briefly during an intercurrent appendicitis, in a 9-year period in the case of Ayres (ADS 47 296, 1943)

The cause is not known. Treatment is usually neglected or symptomatic only

## LICHEN STRIATUS

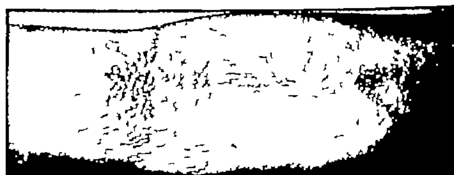
Lesions of linear configuration are seen in various dermatoses, the majority of cases being examples of nevus unius lateralis, lichen planus, or psoriasis but some examples of a simple dermatitis, usually lichenoid, deserve separation as a distinct clinical group, according to Senear and Caro (ADS 43 116, 1941) whose review of the literature and 10 cases personally observed form the basis of our description. The onset is sudden, extension of the eruption to form linear bands is rapid, and the eruption disappears under bland treatment or no treatment at all within few months. The upper extremity is the usual location. The patient is usually a child. The elements of the lesions are lichenoid papules primarily small and discrete but not like those of lichen planus. Coalescence results in patches of erythematosquamous dermatitis. The bands may be continuous or segmented and irregular in width. They are relatively asymptomatic. When they involute, they leave no trace. Histologic changes are nonspecific. The cause is unknown. See cases of Johnson (ADS 53: 51, 1946) Rothman and Niederman (ib. 54: 748, 1946) and Pinkus (JInvD 11 9 1948)

## LICHEN RUBER MONILIFORMIS

The papular lesions of this extremely rare dermatosis are arranged in narrow beaded bands running more or less parallel with each other in the long axis of the extremities. Wise and Rein (ADS 34 830 1936) reviewed the subject exhaustively and were convinced that Kaposi s original case and their own, of 17 recorded instances,

a e alike The dissimilarities with lichen planus, which they aver is in no way related in fact with Morbus moniliformis lichenoides, the title they prefer, include the keloidlike lesions and the absence of the histologic structure of lichen planus. After autopsy of this patie t they (ADS 38 ‗31 1938) were still unable to explain the nature of the disease

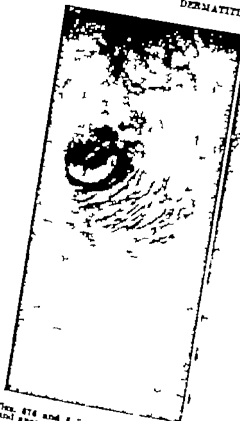




Figs 4 2 4 4 and 473 —Lichen ruber moniliformi bdomen, axillary region and antecubital skin, showing typical eruption (Wise and Rein ADS 24 ‗‗‗, 1931)

## LICHEN SCLEROSUS ET ATROPHICUS

**Symptoms.**— The characteristic lesion is an irregular often polyg onal flat topped, white papule of a color comparable with ivory or mother-of pearl The papules are firm neither elevated nor depressed, or only slightly elevated Generally no areola is present but a rosy or mod erated pigmented areola may surround the papules. These may be discrete or grouped and most cases present both types. When grouped to form plaques, the outline of the individual papules forming the plaques can be determined Each papule has on its shining smooth surface from one to several dark, horny comedo-like plugs, or minute bead-like depressions which show the sites of former plugs. These are situated at the pilose baceous or sweat pore orifices and are important from the viewpoint of diagnosis, wrote Ormsby quoted by Montgomery and Hill (ADS 49 735





Figs. 876 and 877.—Lichen sclerosus et atrophicus, umbilical lesions of … and smooth … lesion of … ... of 63 … Montgomery and Hill … 58 1940.)

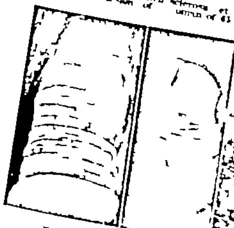




Fig. … Fig. … Montgomery and Hill … keratotic … plugs … Montgomery …

1940) whose report is the major source of our description. The disease is of insidious onset with minimal subjective symptoms, affecting middle-aged and older persons as a rule, women several times as frequently as men. It evinces preference for symmetry of location and involvement of the genital and perianal umbilical, anterior thoracic, scapular and anterior wrist regions. Similarity to morphea and to atrophic lichen planus is considerable. Depigmentation and sharp delineation are features, and, while induration is palpable in the early stages, when the lesions may be somewhat edematous, atrophy generally eventually ensues, with fine wrinkling of the surface. The formation of bullae is not unusual, liability to this phenomenon being comprehensible from the microscopic alterations. When separation of the epidermis occurs, in the same manner as in epidermolysis bullosa, the lesions are painful and may become infected. An extreme example was reported by Gottschalk and Cooper (ADS 55 433 1947) and another by Anderson (ib 49 423 1944) The 3 patients of Laymon (ADS 52 361 1945) were girls under 6 years of age. Carcinoma does not arise from the vulvar lesions of lichen sclerosus, insisted Wallace and Nomland (ADS 57 240 1948)

**Balanitis Xerotica Obliterans** was shown to be lichen sclerosus affecting the glans penis by Laymon and Freeman (ADS 49 57 1944) who sought and found other lesions in 4 of 6 patients whose penile involvement was their complaint When the glans is affected sclerosis and contracture of the meatus result interfering with micturition and requiring dilation or surgical enlargement of the orifice

**Histologically** the typical change is lymphedema in the upper cutis with non mucinous homogenization and edematous alteration of the connective tissue fibers beneath the epidermis Elastic tissue fibers are separated, without destruction from the epidermis, and there is a lymphocytic, plasma and mast cell infiltrate in the midcutis beneath the area of edema. Deeper blood vessels are not *obliterated* a *distinction from morphea*. Epidermal changes are apparently secondary and comprise hyperkeratosis with keratotic plugging of follicles and dermal appendages, atrophy and flattening and loss of the rete ridges. Mild liquefaction degeneration of the basal layer accompanies the superficial dermal lymphedema.

**Treatment**.—Since the cause is unknown, effort is symptomatic, and, most cases being asymptomatic little is to be offered the patient. Friction and trauma should be avoided lest they provoke bulla formation. When bullae have formed talc and protection generally suffice to enable healing to occur Vulvar cases resemble kraurosis and are sometimes symptomatically distressing but treatment other than vulvectomy has been palliative and on the whole unsatisfactory Estrogen applied topically persistently as Premarin cream is curative according to Anderson (Trans SocInvD 1946) cf. Cole (ADS 44 560 1941)

## PSORIASIS

**Symptoms**.—Psoriasis is a chronic, relapsing disease of unknown cause, characterized by the eruption and persistence of reddish, rounded lesions, usually dry and covered with silvery imbricated scales. The disease affects persons of either sex and any age It commonly appears in early adult life, first in the scalp then as a symmetric eruption which involves by predilection the extensor surfaces of the limbs, particularly elbows and knees. The primary lesion is a flat topped papule, which quickly becomes covered with a thin, whitish scale. *Papules enlarge centrifugally*



Fig. 681



Fig. 682

Fig. 681.—Acute guttate psoriasis.
Fig. 682.—Psoriasis, thick lesions of long standing. (Dr Howard Fox.)

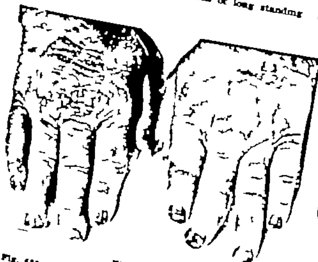


Fig. 683

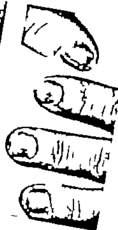


Fig. 684

Fig. 683.—Arthropathic psoriasis, showing psoriasis and bony deformity
Fig. 684.—Psoriasis of nails



Fig 685 and 686.—Psoriasis (Dr J P Guequierre.)

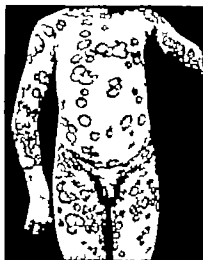


Fig. 687



Fig 688.

Fig 687 —Psoriasis of scalp and body (Dr A. B Cannon.)
Fig 688 —Psoriasis, guttate. (Drs. Kessler and Kessler)

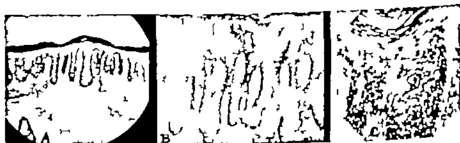



Fig. 689 —Psoriasis, histologic lesion. *A*, An acute lesion *B*, a chronic lesion *C* psoriatic microabscesses in epidermis. (Dr Stuart W )

and neighboring lesions are likely to coalesce The eruption may be sparse, diffuse, or even generalized. When a scale is scraped off, torn tips of hypertrophied and inflamed papillae are exposed, and minute droplets of blood ooze out, the bleeding points typical of the disease. Central portions of some patches may heal so that circinate and arcuate lesions result. Itching is the exception. The lesions are generally dry throughout their course. The patients are remarkably healthy looking individuals as a rule and are not ill with their disease, excepting those with arthritic accompaniments. The eruption may practically disappear in the summer to reappear in the winter or spring (Madden MinnM 22 381 1939) Although psoriasis is usually slow in its development and chronic in its course, it occasionally develops acutely with a more or less widespread, generalized eruption. The scalp manifests discrete patches, a difference from seborrheic dermatitis. Hair loss does not result Occasionally the disease is confined to the scalp or is so limited in distribution for a number of years. The palms and nails are sometimes attacked but the backs of the hands and fingers usually escape. The hands alone may show the eruption, which can then be identified best by biopsy (Caro and Senear ADS 56 629 1947) On the face or scrotum, psoriatic lesions may give rise to redness, swelling induration, and pain, the usual scales being absent.

Once established, the disorder persists, with remissions and intermissions for many years. On disappearing the lesions leave no trace excepting perhaps temporary pigmentation Complete remission is rare. During acute eruption the skin is vulnerable so that the appearance of a new lesion is likely to be incited by an injury accidental or experimental in origin, the Köbner phenomenon. The injury must affect the papillary layer not merely the epithelium As a lesion enlarges, the central part tends to undergo resolution within the cleared and central region, experimental irritation fails to incite new eruption.

**Pustular Psoriasis** is rare. During the interim stage, the lesions resemble those of ordinary psoriasis. During the acute stage, they become larger more numerous, and painfully inflammatory Ephemeral, sterile, intraepidermic pustules appear in the plaques (Mc Kee and Foster ADS 34 33 1936) See Recalcitrant pustular acrodermatitis, p. 179

**Arthropathic Psoriasis.**—The relationship of psoriasis with arthritis is interesting but unexplained. There is close correlation of the exacerbations and remissions of the skin manifestations with the articular symptoms. The arthritis characteristically involves both large and small joints, with especial severity in the terminal interphalangeal articulations (O'Leary: PSMMC 2: 90 1927)

**Psoriatic Exfoliative Dermatitis.**—In rare instances psoriasis becomes universal. In the 18 cases of Goeckerman and O'Leary (J 99 2102, 1932) precipitating causes appeared to be arsenic internally and irritating drugs externally or both, in 14 patients, intercurrent infection in 3, and pregnancy in 1 Although the course tends toward stubborn chronicity they obtained satisfactory therapeutic results in 9 cases within 60 days by means of rest and soothing measures.

**Etiology**.—The cause of psoriasis is not known. It is a common disease Familial incidence occurs in about 30 per cent of the cases, and inheritance is a factor (Lerner JInvD 3 347 1940) The disease is only slightly infectious if at all Borderline cases similar to seborrheic dermatitis occur Many investigators believe that psoriasis must be caused by a parasite Defective liver function has been suggested as a possible cause, and defective fat metabolism is hypothesized by some but Lewinn and Zugerman (AmJMSc 201 703 1941) detected no significant changes in fat tolerance tests. Dodds et al. (BJD 54 212 1942) also found no

blood fat abnormalities. Yet psoriatic prisoners of war cleared on the starvation regime of their imprisonment in many instances during World War II. Extreme restriction of diet with respect to carotene and vitamin A cleared or improved several patients of Hoffmann et al. (NEngJM 236 933, 1947)

**Pathology**.—The inflammatory process probably begins in the papillary layer of the dermis, changes in the epithelium being secondary. The Malpighian layer is thickened, but only in the interpapillary regions. Vascular changes and cellular extravasation are more pronounced in older lesions. Cellular infiltration is greatest in the vicinity of coil gland ducts and hair follicles, and consists for the most part of lymphocytes and small round cells. Wandering cells and microabscesses of Munro (AnndeD 29 961 1898) occur among the epidermal cells overlying tips of papillae. Linear air spaces in the parakeratotic horny layer account for the silvery appearance of the scale (Burks and Montgomery, ADS 48 479 1943). Both punctate and leuconathic onychial changes in psoriasis are due to wavy layers of parakeratotic defective onychization analogous to the typical skin changes (Alkiewicz, BJD 60 195 1948).

**Diagnosis**.—The eruption is usually characteristic. In some cases, however, the disease might be mistaken for seborrheic or contact dermatitis, syphilis, tinea corporis, lichen planus, or lupus erythematosus.

Seborrheic dermatitis almost invariably commences on the scalp as "dandruff" and travels down the medial line of the body. The scalp is involved diffusely rather than discretely as in psoriasis. The scales are greasy and branny. The axillae and other flexures are likely to be involved, and there may be some tendency to ooze. Dermatitis venenata favors the flexural surfaces, is not sharply circumscribed, is often moist, and is itchy. Papulosquamous syphilids are composed of small lesions which come out in crops, do not exhibit predilection for extensor surfaces, are infiltrated and polymorphous, and, in the genital, gluteal, and axillary regions, often become abraded and macerated. Concomitant signs are usually present, such as palpable lymph nodes, bone pains, mucous patches, and a positive serum reaction. Squamous syphilids generally present lesions few in number and asymmetric in distribution. They are crusted rather than scaly, are likely to involve the face or the palms, are often circinate or serpiginous in outline, give rise to atrophic scarring, and are accompanied by a positive serum reaction. In tinea the absence of mother of pearl like scales, the distribution of the lesions, and the demonstrable presence of fungi render differentiation easy. Lichen planus attacks flexural surfaces and gives rise to only slight scaling. Its lesions are violaceous in color and usually itchy. Individual papules are angular and discrete. Bleeding points characteristic of psoriasis are absent. In lupus erythematosus, infiltration is less marked, scaling is slight, demarcation is less sharp, and there is usually scarring. In disseminated lupus erythematosus, facial lesions may resemble those of psoriasis, but body lesions are erythematous or erysipelas like, and constitutional symptoms of some severity are present.

**Prognosis**.—It is not especially difficult to clear an attack, but freedom from recurrences cannot be promised. Lesions which have existed only briefly are more amenable to treatment than those of long standing. Psoriatics do better in a warm, dry, sunny climate.

**Treatment**.— Psoriasis is the disease of specialistic frustration (Murrell and Murrell, SMJ 40 855 1947). While cure cannot be promised, diligent effort and persistence until all lesions are eradicated are to be encouraged. Sometimes the disease does not recur after complete clearing has been attained. The psychologic aspect must not be neglected, for most patients are at least as discouraged as their physician. Watch the tempo of the disease, advised the Murrells, soothe the acute and push the chronic vigorously. The patient benefits from hygienic living, adequate rest, and appropriate attention to concomitant ailments including the elimination of foci of infection.

External remedies are essential, and internal agents are rarely required. We doubt that any medication given by mouth or injection has been discovered which alone is effectual or as an adjuvant possesses dependable value. Mild cases respond promptly and the eruption can be removed within 2 to 6 weeks; moderate cases require 1 to 3 months, while extensive

Fig. 690.

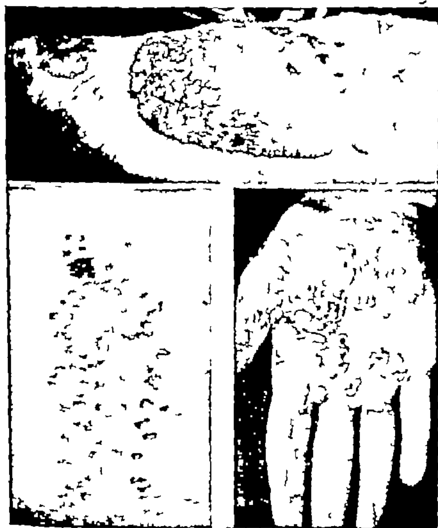


Fig. 691. Fig. 692.

Figs. 690-692.—Fig. 690. [illegible] psoriasis, forearm. Fig. 691. Acute psoriasis [illegible] in the [illegible] scar of a caesarean section. Fig. 692. Psoriasis of the palm (unusual).

and long-standing cases are obstinate. Excessive alcohol, tea, coffee, tobacco, and animal fats are never beneficial. Arsenic in the form of Fowler's solution or sodium cacodylate is a time honored internal remedy but we rarely prescribe it. Arsphenamine is valueless. Massive doses of vitamin

D were given by Ceder and Zon (P H Rpts. 52 1580 1937) who reported helpful effects in 15 cases, 1 of which was arthritic. Anorexia, nausea, malaise and bladder irritation were among the toxic symptoms. Thyroid extract is helpful to any patient who needs it, if he needs it regardless of his other troubles which may include psoriasis. Low fat diet is of dubious value Many other remedies, including foreign protein, autohemotherapy all varieties of vitamins, sarsaparilla extract (Saunders ADS 50 23, 1944) soybean lecithin (Gross and Kesten ADS 47 159 1943) lipocaic (Stewart et al JInvD 2 218 1939) salicylates, bismuth, antimony and gold have been tried and varyingly assessed. We no not use them. See Madden (J 115 586 1940) Wise and Sulzberger (YBD 1940 p 1) Saunders (NoWM 41 135 1942) Symposium (JInvD 4 399 1941)

EXTERNAL APPLICATIONS.—Reducing agents such as chrysarobin, dihydroxyanthranol coal tar ammoniated mercury and betanaphthol are efficient In mild cases, the lesions can often be made to disappear under the action of the official ointment of ammoniated mercury alone or reinforced with 2 to 5 per cent salicylic acid, and applied night and morning. Ointments are best applied with a stiff brush Chrysarobin is the most effective agent It is potent provoking erythema and even vesiculation like sunburn, and its use entails dangers of conjunctivitis, ocular damage and toxic nephritis.

| | | |
|---|---|---|
| R | Chrysarobin | 4.0 |
| | Petrolatum | to 30.0 |

Sig Twelve per cent chrysarobin in petrolatum. Rub in b.i.d. *Avoid eyes with care.* [This irritant is promptly counteracted by applications of 1:3,000 aqueous solution f potassium permanganate ]

Dihydroxyanthranol acts like chrysarobin and is used in strengths of from 0 2 to 2 0 per cent prescribed as Anthralin ointment.

*Dreuw s formula is a popular one*

| | | |
|---|---|---|
| R | Chrysarobin | |
| | Oil of birch tar | of each 8.0 |
| | Salicylic acid | 4.0 |
| | Green soap | 4.0 |
| | Petrolatum | to 60.0 |

The combination is of no greater value than chrysarobin alone.

To secure best results the patient must give himself up to treatment The ointment is thoroughly rubbed into the patches twice daily and the treatment is continued until the skin around all of the spots has become considerably inflamed. Five per cent crude coal tar in lanolin and petrolatum may then be substituted for a few days. Then the patient is given a bath, and the entire surface is inspected. The remaining traces may be eliminated ordinarily by means of tar ointment.

Chrysarobin 3 per cent in chloroform is a remedy of considerable virtue, being not so messy as the ointment. It must be pushed by repeated applications until the skin becomes swollen and sore though blistering should be avoided A patient requires instruction until he becomes familiar with the chemical

Psoriasis of the scalp is usually treated with an ammoniated mercury salicylic acid salve, supplemented by frequent shampoos. Carbowax 1500, being easily washed out is a good vehicle here. In a hospital with skilled

nurses and an intelligent patient chrysarobin may be used on the scalp with excellent effect although it is dangerous to the eyes.

Psoriasis of the nails is exceedingly obstinate Ammoniated mercury ointment, alone or combined with salicylic acid is helpful. Roentgen therapy is valuable here Popp and Addington (Radiol 36 96, 1941) would direct the beam at the whole hand and wrist including the tips of the fingers.

ULTRAVIOLET IRRADIATION.—Goeckerman (NoWM 24 229 1925) used ultraviolet light and crude coal tar ointment

| | | |
|---|---|---|
| ℞ | Crude coal tar | 6.0 |
| | Lanolin, to mix | |
| | Zinc oxide | 30.0 |
| | Petrolatum | 100.0 |

This is smeared on thick, left 24 hours, then wiped off with mineral oil, leaving purplish a brown stain. The stained patches are exposed to the quartz lamp, beginning with an exposure that avoid reaction. Daily exposures for a half minute each time for 4 to 5 times, are lengthened more rapidly as tolerance increases. Gradual tanning is the object

Goeckerman's method is well standardized and effective, as attested by Brunsting (MichSMSJ 42 546 1943) It is less effective in nummular psoriasis of recent origin and in exfoliative involvement (O'Leary Canad MAJ 48 34 1943) An ambulatory modification is used by Kelm, who prescribes tar in a cetyl alcohol emulsion base for evening use, a tar bath in the morning and a daily visit to the physician's office where liquor carbonis detergens is applied and ultraviolet light administered. The patients of Ellis et al (JInvD 10 455 1948) did well on daily paintings with liquor carbonis detergens whether ultraviolet light was or was not used

ROENTGEN THERAPY has great value in psoriasis of the nails and scalp and also in promoting the disappearance of thick, rebellious lesions. Small doses suffice and enhance the effects of other efforts made simultaneously Precautions must be taken with respect to cumulative dosage and to dosage of large areas with deleterious effects on hematopoiesis.

## PARAPSORIASIS

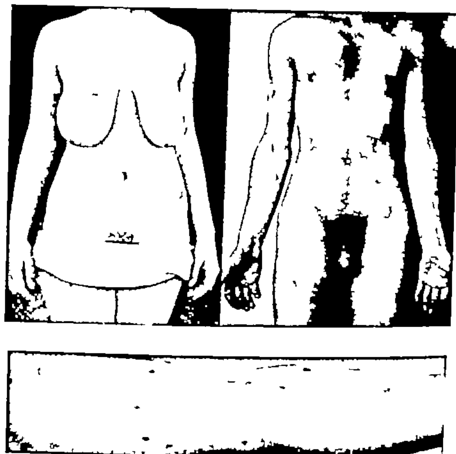
**Parapsoriasis. The Chronic Resistant Macular and Maculopapular Scaly Erythrodermas.**—An ill defined and probably etiologically heterogeneous group of dermatoses is described by this title suggested by Fox and Macleod (BJD 13 319 1901) Cases may be reminiscent of a combination of the features of psoriasis lichen planus, seborrheic dermatitis and early mycosis fungoides Reddish, circumscribed plaques of slow evolution scattered irregularly over the body characterize eruption so classified. Wise (NYAJM 25 901 1925) recommended that the various names recognized by discriminating specialists be retained until better understanding is available be distinguished them as simply as it could be done. Histologic studies were recorded by Montgomery and Burkhart (ADS 40 [illegible] 1939)

PARAPSORIASIS EN PLAQUE [illegible] is actually the early stage of mycosis fungoides in a significantly high proportion of the cases (Keil ADS 37 465, 1938) If early mycosis fungoides were surely identifiable parapsoriasis would be diminished to that extent

PITYRIASIS [illegible] AND [illegible] of Mucha and Habermann is a self limited and [illegible] disorder in which the rash simulating a secondary syphilid or pityriasis rosea, generalized and papula with tendency to crusting, necrosis and hemorrhage and pigmentation and [illegible] form scarring follow the disappearance of some of the lesions Ramos and [illegible] (ADS [illegible], 1931)

PITYRIASIS [illegible] (PARAPSORIASIS GUTTATA) is pruritic enduring unresponsive to treatment and others [illegible] different from the acute form, which was thought to be [illegible] of the chronic by Gross (ADS [illegible] 33, 1931)

Parakeratosis variegata, the retiform variety of parapsoriasis, was discarded by McCarthy (ADS 45 81 1942) who believed that modern diagnosis of such cases would result in their being distributed among the unusual forms of lichen planus or among other varieties of parapsoriasis.



Figs. [illegible].—Parakeratosis variegata. (Cases of Dr Paul Gross and Drs Wise and Sulzberger.)

## EXFOLIATIVE DERMATITIS

**Symptoms.**—Exfoliative dermatitis is the descriptive title given to any desquamating dermatosis of extreme distribution and inflammatory appearance. The class is etiologically heterogeneous, for generalized or universal involvement may be due to diseases of the following varieties, descriptions of which should be reviewed from this standpoint:

Contact dermatitis (fabric finish, medicinal)
Dermatitis medicamentosa (arsenicals especially)
Atopic dermatitis (including food and inhalant allergy)
Bacterial dermatitis coccic primary or secondary
Dermatomycosis (tinea imbricata, moniliasis, dermatophytid)
Avitaminosis and hypoproteinosis

Psoriasis, seborrheic dermatitis, parapsoriasis lichen chronicus simplex
Lymphoblastoma (malignant erythroderma)
Combinations of the above (contact dermatitis plus focal infection etc.)

The principal clinical forms are those of Wilson Brocq and of Hebra

**Exfoliative Dermatitis (Wilson Brocq)** may be either primary or secondary In the primary variety, the eruption appears suddenly and may be either patchy or universal Pinkish or reddish at first and symmetrically distributed, the affected areas become covered with thin, flaky loosely adherent grayish or brownish scales. From the volar surfaces the corneous layers are sometimes thrown off in glovelike casts. Nails and hair both may be shed There is usually little itching although the skin is tender and the patients complain of tension stiffness, chilliness, malaise and debility The amount of scaling varies but is profuse, and a liter may be exfoliated within each 24 hours. Acute cases exhibit little cutaneous thickening but in long-standing ones infiltration may be considerable. There is no vesiculation or exudation as a rule An outbreak lasts for several weeks or months, and relapses are likely

In the secondary variety the condition follows various scaly affections such as *dermatitis venenata, psoriasis, and seborrheic dermatitis. It is probably* often the result of the use of irritants like chrysarobin, ammoniated mercury and salicylic acid. Malaise chilliness, and fever are common complaints. We have seen a patient with mercurial exfoliative dermatitis develop a fever of 6 F in 6 hours following Merthiolate wet dressings this, in fact, was the evidence which led to correct diagnosis. Oozing is likely to be a feature and paroxysmal flares with violent itching and distress are observed. Furunculosis and abscesses may make their appearance. especially in the axillary and other hairy regions, often as a complication of the use of ointments, which cannot long be applied safely to these regions even if the skin is normal Lymphadenitis, leucocytosis, and relative eosinophilia are generally found.

**Pityriasis Rubra (Hebra)** —This rare chronic dermatitis is characterized by involvement of the entirety of the body surface, general lymphadenopathy only slight infiltration and pruritus, pigmentation, eventual glossy atrophy and unremitting duration until death ensues. Weakness and emaciation are progressive The soles are likely to become too atrophic and fragile to support walking Abscesses are common. The patient complains of chilliness, and he huddles beneath the bedclothes. No area of skin is likely *to become normal even temporarily during the course of the* disease Death results usually from bronchopneumonia.

**Etiology**.—Exfoliative dermatitis occurs usually in middle life and prefers males in a ratio of 3 to 1 We believe that many cases commence as banal inflammation upon which is superimposed dermatitis of contactant intolerance and this becomes secondarily infected, and perhaps sensitized, by pathogenic bacteria and fungi Focal infection plays an important role

**Pathology**.—The papillary bodies are enlarged and elongated, and both they and the subjacent corium are moderately infiltrated with leucocytes. Cellular exudate is greatest in the vicinity of the vessels and around the coil gland ducts. The epidermis is thinned, irregularly hyperkeratotic and *parakeratotic* and scaling The benign hyperplasia of lymph nodes occurring in exfoliative dermatitis may be accompanied by



Fig. 699



Fig. 700.

Fig. 699.—Discoid lupus erythematosus.
Fig. 700.—Discoid lupus erythematosus. (Dr W Herbert Brown.)



Fig. 701.

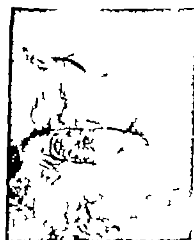


Fig. 702

Fig. 701.—Classic discoid lupus erythematosus.
Fig. 702.—Atrophic lesions of discoid lupus erythematosus with squamous carcinoma of the lip on the lupus scar in a man of 28 years.

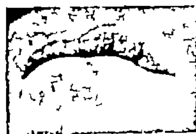


Fig. 703.

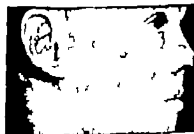


Fig. 704.

Fig. 703.—Discoid lupus erythematosus affecting the upper lip.
Fig. 704.—Atrophic scarring of discoid lupus erythematosus. (Dr Gasquierre.)

the patches are sharply defined, and cicatricial alopecia is the sequel. Mucous membranes are involved in about 25 per cent of the cases. The lesions may consist only of slight thickening with duskiness and scaliness of the affected part, or some abrasion of the surface may be present. The mucous surfaces which are most commonly attacked are those of the lips, eyelids, cheeks, and tongue. Healing is followed by atrophy. Symptoms are slight, described by the patient as burning or tension with little itching.

**Etiology.**—The cause is unknown. Circulatory disturbances and actinic trauma are predisposing factors. Sunshine is extremely harmful in these cases. The majority of the cases occur in women. The incidence, sites of predilection, geographic distribution of cases, and other etiologic aspects were studied by Gahan (ADS 45 685, 1133 1942) whose statistics are interesting though not revealing. The hypothesis of vasculoallergic response to microorganisms appealed to Stokes et al. (AmJMSc 207 540 1944). Focal infection was generally present in the cases of Cerri (abs YBD 1939 p. 168) and its elimination was generally beneficial.



Fig. 161.—Lupus erythematosus, discoid: section showing hyperkeratosis, follicular plugging, colloid in body of dermis, dense perivascular lymphocytic infiltrate. (Dr Hamilton Montgomery.)

**Pathology.**—Early changes consist in dilation of the superficial vessels, followed by extravasation first of leucocytes, then of lymphocytes and monocytes (Montgomery, JInvD 2 343, 1939). Epidermal changes, probably secondary to dermal inflammation, are of diagnostic value, comprising irregular hyperkeratosis, keratotic plugging of follicles and ducts, preservation of the granular layer, acanthosis side by side with atrophy of the prickle cell layer, and liquefaction necrosis of the basal layer. Infiltration is chiefly lymphocytic and is located about the vessels and appendages. The cutis is edematous, and elastic tissue is damaged in infiltrated regions. Walls of deeper blood vessels do not show proliferative or obliterative change. Atrophic scarring characterizes the late stages.

**Diagnosis.**—The well-defined type of lesions, their history course shape color consistency and distribution, together with the presence of atrophy should prevent error

Contact dermatitis, psoriasis seborrheic dermatitis, superficial epithelioma, lupus vulgaris, and syphilis are to be excluded. Eczematous lesions are itchy not sharply marginated, often vesicular, and do not scar In psoriasis, scale formation is prominent, and bleeding points can be demonstrated. Seborrheic dermatitis is seldom sharply defined, and scarring is never present Lupus vulgaris generally begins in childhood; the scars are seldom soft and atrophic but are usually rough, corded, and conspicuous; typical apple-butter-colored nodules occur at the margins of a tuberculous lesion. Tubercular syphilids commonly give rise to more or less scarring, but the cicatrices are smooth and unmarked by patulous gland orifices. The lesions develop rapidly individual nodules are usually present, there is a tendency to ulcerate, and the blood test is positive Epithelioma has a definitively sharp margin when closely scrutinized.

**Deep, Hypertrophic, Discoid Lupus Erythematosus** is a recognizable variant in which the lesion are more or less vegetative with deep pits and depigmentation (Bechet ADS 45: 33 194 ) Papular and nodular forms are also seen (Irgang: ADS 43 281, 1941) The firm sharply outlined, movable subcutaneous tumors of lupus erythematosus profundus were said by Arnold (ADS 57 196, 1948) to resemble sarcoid clinically but to consist histologically of compact periglandular and perivascular lymphocytic infiltrations. Arnold's case not hypersensitive to tuberculin or responsive to bismuth, was cured by intravenous gold.

**Prognosis**—Discoid lupus erythematosus is a chronic disease capricious and erratic in its course with relapses and occasional recurrences likely to occur Occasionally the lesions disappear spontaneously Sometimes new patches develop and older ones extend despite the use of approved therapeutic measures Onset at age 20 months occurred in Becker s patient (ADS 50 424 1944), in the discussion of which Ormsby said the prognosis in the young child is favorable Dissemination is possible and is ominous when it occurs. Approved therapy itself entails dangers

**Treatment.**—The eradication of foci of infection is a valuable measure Foreign protein therapy is hazardous. The patient should perhaps be advised to avoid coffee tea, chocolate cream and alcohol.

In choosing a local agent it is wise to begin with mild, soothing lotions As good as any is calamine lotion with 0.5 per cent of phenol Patches may be cleansed by means of mineral oil and must be protected from sunshine Remedies such as 10 per cent Ichthyol in collodion or in ointments, or weekly applications of pure phenol or of a saturated aqueous solution of lactic acid may be tried Hollander s combined method sometimes proved helpful the patient is given quinine sulfate, 0.5 gm. t.i.d. daily for from 5 to 7 days each evening the lesions are painted with tincture of iodine at the end of the period the treatment is discontinued until the crusts have become detached Then, if necessary another course of treatment is instituted. Solid carbon dioxide is excellent in chronic discoid cases. One application under moderate pressure for 2 seconds may suffice: it is our first choice Roentgen, radium and ultraviolet irradiation are worthless or harmful

Intramuscular injections of bismuth preparations have been highly recommended Tolman (NEngJM 219 688 1938) judged from his review of 122 cases that bismuth is as good as gold Gold and sodium thiosulfate is given intravenously and should not be used indiscriminately The agent is a valuable one yet of 31 patients treated with gold, 74 per cent relapsed (Callaway and Stokes ADS 37 627 1938) An initial dose of 5 milligrams of gold sodium thiosulfate is probably safe. Weiss et al (ADS 35

1074 1937) found that the discoid cases as well as the disseminated ones tend to have leucopenia When giving gold the white blood cell count should be followed with care and caution A patient may respond to doses of 50 to 100 mg if unresponsive to 10 mg said Wise (ADS 40 668 1939) but the hazard of thrombocytopenia must continually be born in mind. Gold was not found spectroscopically in active lesions of patients under gold therapy but it was present in the healed scars of patients so treated (Bernhauer et al ADS 50 315 1944)

Gold sodium thiosulfate, 0 06 c c of the 1 per cent solution with procaine may be injected at each of several sites about the periphery of the lesions without complication curing some patients in whom intravenous gold has failed, according to Monash and Traub (ADS 50 318 1944)

Barber (Lancet 1 583 1940 BJD 53 1 34 1941) recommended the elimination of focal infection, then the administration of sulfonamide in a dose seldom exceeding 1 tablet 3 times a day A febrile reaction and malaise for 8 to 14 days were expected, he said and a generalized scarlatiniform eruption Herxheimer like was not to be considered alarming, although during such a reaction the drug should be stopped. He thought this treatment beneficial when the case depended on streptococcic infection but without value when the cause was tuberculous (Glyn Hughes and Spence (BMJ 2 741 1940) confirmed his findings while they acknowledged the hazards. Bismarsen was the choice of Weiss et al (ADS 44 1009 1941) who admitted the necessity of constant observation of cases so treated.

Mapharsen recommended by Sulzberger helped a patient of Baer (ADS 49 131 1944) and several patients of Hyman (ib 53 26, 1946) Goldberg (ADS 52 89 1945) gave 0 02 gm Mapharsen intravenously twice a week to 21 patients, who he said, promptly improved

Suramin (germanin) the hazards of which are emphasized, was specularly helpful in a case of Costello (ADS 54 736 1946)

**Disseminated Lupus Erythematosus** occurs in two types (1) gradual dissemination of lesions which resemble the discoid, and the disease may subside or by a long debilitating course lead to death and (2) acute dissemination with flares in which cutaneous lesions resemble erysipelas or erythema multiforme and visceral involvement is productive of fever prostration and the likelihood of death within a few months. The lesions range from 1 to 10 cm in diameter and are usually superficial and bright red in color Occasionally they are infiltrated or bullous in character resembling eruptions occurring in some cases of dermatomyositis. The regions commonly involved are the face V of the neck and dorsa of hands and feet, but no part of the body is exempt Mucous membranes are frequently attacked. Lesions may come in crops some patches persisting indefinitely and others disappearing spontaneously with little scarring, only to be replaced from time to time by new patches The patient is ill and loses weight The course is erratic with unpredictable remissions. Fever is of had omen Leucopenia or leucocytosis may occur The disease is diagnosticable in the absence of skin lesions, being a systemic disorder of unknown cause with variable pathologic picture and a variable symptomatology (Reifenstein \\ EJM 4- 227 1942)

**Visceral Lesions** noted by Rose and Goldberg (MCNAm 19 333 1935) and attributed by them to widespread vascular damage produced symptoms including fever of septic type weight loss weakness, bone and joint pains, abdominal pain headache cough dyspnea, hemoptysis, nephritis albuminuria, erroneous endocarditis disseminated telangiectases hemorrhagic or fatty hepatitis, terminal bronchopneumonia, pulmonic abscess tuberculous or nonspecific lymphadenitis focal and metastatic infection, and

retinitis, all of which were observed, though not in one patient. Blood cultures are sterile. Baehr et al. (AmJPath 11: 881, 1935) reported 23 cases studied at necropsy of a diffuse disease of the peripheral circulation usually associated with lupus erythematosus and endocarditis. The basic pathologic change seemed to be a necrotizing injury of the small vessels, with thrombosis and hemorrhage 13 of the 23 had verrucose endocarditis, glomerular capillaries were occluded, forming hyaline cords described as wire loop lesions. The various organic changes have in common a pathologic involvement of collagenous tissues such as may be induced by repeated intravenous infections of foreign protein, according to Klemperer et al. (APath 32 569 1941 J 119 331 194 ; NYSJM 42: 2225 1942; J 134: 1169 1947) representative of colloid imbalance with variable degrees of disturbed function, not necessarily related to allergy



Fig 706



Fig 707

F 06.—Acutely disseminated discoid lupus erythematosus, exacerbation being followed gold therapy and exposure to sunlight Forehead was protected from light by hat (Urbach BJD 31 213 1920)

Fig. 707.—Disseminated lupus erythematosus, cute. (Dr J P Gosquierre)

The features of a case may emphasize any combination of the following: pleuritis, pleural effusion, pericarditis, pericardial effusion peritonitis, perisplenitis, pneumonia, nephritis nephrosis hyperplasia of bone marrow lymphoid hyperplasia, myocarditis, valvulitis and miscellaneous vascular lesions, Laipply and Longley (ClinBullWestRes Univ 4 31 1940) observed. There were high sedimentation rates and marked increases in serum gamma globulin in patients of Coburn and Moore (BullJHH 73 196, 1943) and some showed false positive Wassermann test (see White AmJS 31 235 1947) While most patients are female, the 17 year old boy of Gingler and Fox (AlntM 65; 76 1940) suffered polyarthralgia especially and died with pericarditis, leukopenia, and renal damage following the removal of a focus of infection. The woman, aged 31, of Michelson (MinnM 22 565, 1939) developed her disease following a sunburn, and it became generalized with fatal outcome after a test dose of ultraviolet light. Periarterial fibrosis of the spleen occurred in 15 of 18 cases of Kaiser (BullJHH 71: 31 1942)

Cardiac lesions of the atypical verrucous sort characterizing the Libman Sacks syndrome in which blood culture is sterile and the myocardium shows no Aschoff bodies, existed in 4 of the 23 fatal cases studied by Gross (AmJPath 16: 375, 1940) Adrenal insufficiency (Jager: ADS 46 362, 1942) and retinal damage (Maumenee AmJOphth 23 971 1940) are among the features which have incited publication of cases. Renal changes terminating in uremia were reviewed by Stickney and Keith

(AIntM 66 643 1940) who noted resemblances only not identity with glomerulonephritis. The urinary findings are remarkable in that everything may be found, red blood cells, all kinds of casts, and protein, a diagnostic heterogeneity (Krupp: AIntM 71: 54 1943) Prognosis is poor in pregnancy

**Treatment.**—It is dangerous to attack foci of infection, although they are usually present transfusion likewise usually fails to benefit. Persistent pyrexia, as well as severe edema, is an earmark of the fatal cases (O'Leary AIntM 17 637 1934), loss of weight is not marked until the case is advanced. Engman (ADS 35 68, 1937) stressed the relationship with fatigue and overwork, the occurrence of leucopenia, and the need for rest in the period of onset, which may be insidious. The bed, cod liver oil, and a nutritious diet are especially valuable agents in combating the disease. Sulfonamides have been variously assessed Weiner (ADS 41 534, 1940) helped 2 of 4 cases Wile and Holman (ib 42 1059 1940) were discouraged by their experience with 7 cases. Penicillin seemed to cure the patient of Strakosch (ib 54 197 1946), but its effects are not reliable. Cannon (ADS 51 26 64, 1945) was enthusiastic about the cures he claimed with 7 per cent tincture of iodine, giving in increasing doses from 3 to 20 drops t.i.d. by mouth and supported by high calorie diet, vitamins, and perhaps transfusions. Liver extract by intramuscular injection was the recommendation of King and Hamilton (SMJ 34 304, 1941) who claimed 6 cures see Cornbleet (ADS 43 829 1941) Sodium para-aminobenzoate seems to help in subacute disseminations (Curtis et al. TransSocInvD 1948) Creatinuria and low 17 ketosteroid excretion led Lamb et al. (ADS 57: 785 1948) to give steroid hormones, which helped some females.

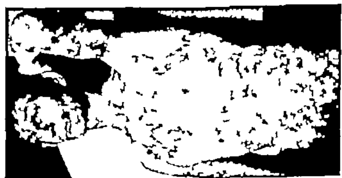
## DERMATITIS HERPETIFORMIS

**Symptoms.**—Dermatitis herpetiformis (Duhring's disease) is a chronic, relapsing inflammatory dermatosis characterized by the occurrence of erythematous, papular vesicular or pustular lesions, which tend to be grouped, are intensely itchy and are followed by pigmentation and atrophic scarring. An attack is usually ushered in by slight constitutional symptoms, seldom severe but in many patients serving as an aura. Itching is exceedingly distressing Sensations of burning and tension also are frequent complaints. The vesicular form of eruption is the most characteristic, but polymorphism is common. The eruption, roughly symmetric, nearly always involves the sacral triangle and the scapular areas. The scalp and extensor aspects of the extremities are usually affected. The lesions develop rapidly in groups and circles which spread by peripheral extension. The vesicles possess thick, tough walls, and seldom rupture spontaneously The patient finds relief in scratching off their tops, preferring pain to itching Scarring and pigmentation are characteristic sequelae.

The disease is a variable and erratic one. Periods of outbreak are interspersed with periods of comparative quiescence Victims become nervous, poorly nourished, debilitated, exhausted and despondent as a result of itching and loss of sleep

**Etiology.**—The cause is not known The disease is comparatively rare occurring oftenest in adult males. No age is exempt, for the patient of Ebert (ADS 48 210 1943) was 3 years old, and Wilson's (ib 44 58 1941) only 2 weeks. Most of our patients have been outdoor people who have associated considerably with domestic animals. Intolerance of halogens, especially iodides, has long been known to exist in dermatitis







Figs. 708-710.—Dermatitis herpetiformis.

herpetiformis Flesher (JInvD 8: 55 1947) noted that patch tests with 20 per cent potassium thiocyanate in petrolatum are also positive and recognized the phenomenon as being due to the swelling of gelatin so as to induce separation of the epidermis by salts of the Hofmeister series. Positive patch and intradermal tests with a pneumococcus from the patient's bronchial secretion were obtained by Callaway and Sternberg (ADS 43 956, 1941) and comparable allergy to a *B coli* vaccine was studied by Swartz and Lever (ib 47 680 1943)

There is much literature but little proved regarding the hypothesis of virus etiology, especially by authors who are confused as to the distinctness of dermatitis herpetiformis and pemphigus.

HERPES GESTATIONIS appears to be true dermatitis herpetiformis peculiar only in its appearance during pregnancy (Howard ADS 28 782, 1933) *Sulfathiazole helped Lewis's patient (ADS 46 841, 1942)* but that of Turner et al. (AmJOG 41: 525 1941) was unresponsive to medicines yet healed promptly after parturition.

**Diagnosis.**—The disease is to be differentiated from pemphigus, erythema multiforme infectious eczematoid dermatitis, scabies, and pediculosis. In scabies interdigital spaces are likely to be involved while the scalp is unaffected lesions are minute blood-capped excoriated papules itching is worse at night and the patient's associates are usually infected



Fig. 111.—Dermatitis herpetiformis. (Dr E D. Sweitzer)

**Prognosis.**—An attack can usually be ameliorated or stopped, but permanent relief can never be promised. The outlook is better in younger patients

**Treatment.**—The patient must obtain rest This can often be obtained by interdicting coffee by giving aspirin, gr v every 3 hours and by urging the patient to lie down every hour of the day that he is not obliged to do otherwise Sodium cacodylate is particularly valuable Doses of 0.5 gm. intramuscularly may be given twice a week. Quinine, autohemotherapy thiosulfate intravenously and hyperpyrexia may be tried Noniodized salt should be used, and not much of that bromides must be avoided. Focal infection should be sought out and eradicated Vaccine made from a focus may be used for desensitization (Callaway SMJ 35 415 1942) Acetarsone 0.5 daily for 3 days per week, may relieve (Cornbleet et al. ADS 52 292, 1945) Penicillin has helped the disease temporarily but the patients of Carpenter and Hall (ADS 51 241 1945)

relapsed when it was stopped. *Iron cacodylate, 0.065 gm. per day for a long time,* was recommended by Weiss. The best internal medication is sulfonamide, sulfapyridine being preferred by Costello (ADS 56: 614, 1947). A small dose may suffice. While due precaution as to possible ill effects must be taken, the patient of Harling (Lancet 1: 503, 1944) ingested sulfonamides for over 3 years with relief and no harm. We had good results in two cases using Fuadin. Locally calamine lotion, to which has been added 0.5 to 2 per cent carbolic acid and 1 to 5 per cent compound tincture of coal tar alleviates. Duhring recommended an ointment containing 5 to 10 per cent sulfur. Bland, soothing greasy mixtures are helpful. *Deep x ray therapy over the spinal ganglia may be tried.*

## IMPETIGO HERPETIFORMIS

This rare disease described by Hebra (WienMWchr 32: 1197, 1872; Lancet 1: 399, 1872) is manifested by a symmetric eruption of pustules which occur in crops, form groups or rings with flat yellow crusts but without ulceration, itch little if at all, and are accompanied by severe constitutional symptoms. The lesions are pustular from the start, being never vesicular. The pustules and the blood are sterile on culture. The eruption may become widely disseminated. Fever, great prostration, leucocytosis, hypocalcemia, and sometimes tetany accompany it. When the lesions heal, an unusual reddish-brown pigmentation is seen. Most patients are pregnant females. *The child when born is free of the eruption but dies soon* (Teslen: ActaD-V 18: 145, 1937). The review of Hall (ADS 50: 10, 1944) should be consulted; the patient he reported was a man whose dermatosis followed lobar pneumonia and healed under sulfonamide therapy. Anderson, discussing Hall's paper, would separate the group of cases not associated with pregnancy but occurring usually subsequent to a severe infection in a seriously toxic patient with a septic fever. Parathyroid extract or vitamin D concentrates such as dihydrotachysterol may be given with hope of benefit (Seberber: DWchr 106: 361, 1938). Although the woman in her fourth month of pregnancy reported by Frank (ADS 40: 253, 1939) was saved by sulfanilamide, her twin infants were promptly aborted.

## PEMPHIGUS

**Symptoms.**—Pemphigus is a *rare, serious dermatosis* characterized by the eruption of successive crops of bullae which develop suddenly often on apparently normal skin. Clinically pemphigus may be separated into 3 types: pemphigus vulgaris, pemphigus foliaceus, and pemphigus vegetans.

**Pemphigus Vulgaris.**—The history of pemphigus is interestingly reviewed by Lever and Talbott (ADS 46: 800, 1942). The onset is likely to be insidious with the development of blebs in a localized region, sometimes mucosal (Oppenheim and Cohen: ADS 46: 201, 1942). A faintly erythematous and edematous rash with marginate lesions resembling *urticaria but almost asymptomatic and less inflammatory* may comprise the background upon which the noninflammatory bullae develop. The local patch may be eczematoid. A widespread eruption of bullae ensues. Lesions may be present practically all the time, new blebs developing as the older bullae dry up and disappear, or outbreaks lasting a few weeks or months are alternated with periods of complete or comparative quiescence. The bullae are 1 to 10 cm. in diameter, several in number, thin walled, translucent, sometimes coalescing. They may be umbilicated or irislike. Zeisler has found the bullae flaccid in the serious cases and tense in the milder ones. They develop suddenly on apparently normal or slightly reddened areas, increase in size little if at all, and are never infiltrated. The distribution of the eruption is roughly symmetric. The mucous membranes seldom escape.



Figs. 712 and 713.—Pemphigus vulgaris, acute in onset

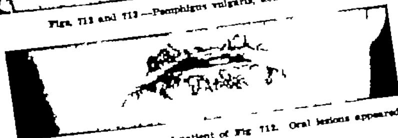


Fig. 714.—Pemphigus vulgaris, lips of patient of Fig 712. Oral lesions appeared first in this case.

Fig 715. Fig 716.

Fig 715 —Pemphigus vulgari (Dr T W Thorndyke )
Fig 716 —Pemphigus vulgari Dr D. H. E. Cleveland )



Fig 717



Fig 718

Fig 717 — Pemphigus vulgaris. (Dr D E H Cleveland.)
Fig 718 — Pemphigus vegetans (Dr W Herbert Brown.)

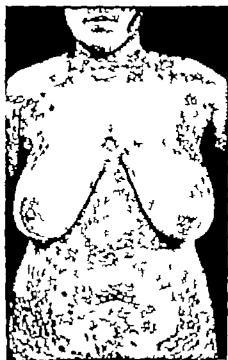


Fig 719



Fig 720

Fig 719 — Pemphigus foliaceus (Dr A B Cannon)
Fig 720 — Pemphigus foliaceus.

*Adhesion between the epidermis and dermis is damaged by subepidermal vacuolation and an accumulation of fluid pushes off the epidermis.* This seems to be due to a lipoproteinous change in the superficial collagen (MacCardle et al ADS 46 517 1943) Pinching and friction provoke such separation. The Nikolski test consists in so traumatizing the skin as a diagnostic procedure.

Itching may be considerable The patient loses strength and becomes an exhausting nursing problem Decaying epithelium stinks, and secondary infection, often terminating in bronchopneumonia takes its toll.

Anemia is progressive the white blood cell count variable, the sedimentation rate high, and sodium chloride calcium and protein of the blood serum are diminished in proportion to the severity and extent of cutaneous involvement (Eller and Kest ADS 44: 337 1941 Lever and Talbott NEngJM 231 44 1944) These changes, with increase of the plasma volume suggest those of adrenal cortical insufficiency and the administration of adrenal cortical extract and sodium chloride may help such patients (Talbott and Coombs ADS 41 359 1940 Talbott et al. JInvD 3 31 1940 Goldzieher ADS 53: 42, 1946) Adrenal lesions were found only in the patients who had received auramin in necropsies studied by Humphreys and Donaldson (AmJPath 17 767 1941) Fatty degeneration and passive congestion of the liver were abnormalities common to 9 necropsies reported by Gellis and Glass (ADS 44 321 1941)



Fig. 721.

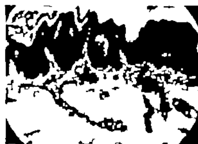


Fig 722.

Fig. 721.—Pemphigus, as by blebs. (Dr Fred W Kime )
Fig 722.—Pemphigus foliaceus.

**Pemphigus Foliaceus** may be more or less characteristic from the beginning, or it may commence with resemblance to pemphigus vulgaris, herpetiform dermatitis, or even exfoliative dermatitis Large fragile flaccid bullae develop rapidly They contain pus from the first They soon rupture leaving a moist raw surface covered with seropurulent fluid Decaying epithelium and exudation give rise to a peculiar sickening odor The course is essentially chronic Exacerbations followed by periods of comparative quiescence are common but the skin seldom clears between attacks.

**Pemphigus Vegetans,** more common in females, begins with eczematoid impetiginoid, or bullous disease generally of the axillae groin, umbilical region, mouth or pharynx (Riordan ADS 53 632, 1946) The genitals, chest abdomen and other regions of the body may become involved Some lesions persist and papillary excrescences resembling

condylómas spring up Ulceration may occur Belisario said that potassium antimony tartrate injections cure this disease.

**Etiology**—The cause of pemphigus is unknown. Welsh (ADS 30 611, 1934 JInvD 7 7 1946) isolated a streptococcus, the intracutaneous inoculation of which produces bullae, but Curtis and Topp (JInvD 9 151 1947) could not confirm these observations. Pels and Macht (ADS 36 1022, 1937) found that the serum of a patient with pemphigus inhibits the growth of seedlings of *Lupinus albus Hartwegi* more than normal serum does. This specific phytotoxicity is diminished or destroyed if the serum is exposed to x radiation, but serums from other dermatoses are not so detoxified and deep x ray therapy over the liver and spleen was followed in 10 cases by clinical improvement attributable to detoxification of the blood, reported Macht and Ostro (UCutRev 51 651, 1947) Grace and Suskind (JInvD 2 1 1939) transmitted through mice a virus isolated from vesical fluid from 4 patients, but its pathogenicity is unproved.

**Pathology**—In the early lesions one finds intracellular edema, intra epithelial vesiculation, and migration of polymorphonuclear leucocytes into the epidermis from the superficial cellular infiltrate in the dermis. The blood picture shows terminal leucocytosis, the proportion of immature polymorphs being a sensitive index of change in the general condition (Grace ADS 55 772, 1947) Eosinophilia diminishes with deterioration. Relative monocytosis is found in the terminal stage

**Prognosis** must be guarded. The patient s condition can usually be temporarily benefited. Almost all victims eventually die of the disease it has been thought (Lever and Talbott ADS 46 348 1942)

**Treatment.**—Large quantities of powder may be applied. One may withdraw fluid from the blebs and inject into them 1 per cent aqueous methylene blue A mouthwash containing benzocaine 5 to 10 per cent, and oil of wintergreen, 0.3 per cent, in emulsion of almonds 90 parts, and mucilage of acacia 10 parts, allays pain (Pillsbury) Therapeutic baths, sometimes the continuous bath are useful we have occasionally been pleased by 1 15 000 mercuric chloride in isotonic saline. Bichloride of mercury possesses some virtue, for Sonnenberg (AnndeD 10: 771, 1939) reported 7 survivals out of 12 patients who were given 1.0 c.c. of the 1 per cent solution intramuscularly each week.

Acetarsone appears to offer the most, empirically Oppenheim and Cohen (ADS 47 40 1943) prescribed the 0.25 gm. tablets to be taken before breakfast at the rate of 2 tablets the first day, 3 the second, and 3 the third, followed by a rest of 3 days then a repetition of the course This is carried on until the patient has received a total approximating 1 tablet per kg of body weight, or 70 tablets. A patient of Goeckerman (ADS 55 691 1947) received over a period of time 225 gm. of acetarsone without ill effect. Carbarsone in place of acetarsone and in similar doses was recommended by Little (ADS 52 397 1945) Carbarsone, 0.25 to 1 gm. before breakfast daily (PABA neutralizes toxicity) Amigen by mouth in adequate amounts, débridement, petrolatum gauze and bland topical antiseptics, were the measures used with outstanding success by Combes et al. (ADS 57 532, 1948)

Wise and Sulzberger (YBD 1934 p 398) thought sodium arsenate of value they gave the 2 per cent aqueous solution intramuscularly in daily ascending doses to tolerance They considered suramin (germanin) dangerous as well as disappointing although it is helpful in some cases.



Fig. 723.—Acute pemphigus. The boy recovered. (Dr R. A. Sparks.)



Fig. 724.



Fig. 725

Fig. 724.—Brazilian pemphigus. (Dr O. G. Costa.)
Fig. 725.—Brazilian pemphigus. (Dr O. G. Costa.)

tholysis lead to the formation of intraepidermal clefts and vesicles, and cutaneous changes seem secondary to the epithelial changes, wrote Pinkus and Epstein (ADS 53 119 1946) While bacteria of possible pathogenicity have been cultured from the le[…]ey are doubtless secondary In treatment zinc stearate[…]d and the avoidance of friction are to be rec[…] therapy is useful. Vitamin A in la[…] (Fraser: ADS 46 326, 1942) […] 1941) Frank and Rein (ib

Mongolian spots are congenital bluish o brownish pigmented spots, generally occurring on the lower sacral areas, but sometimes on other parts of the body. They are asymptomatic, and do not alter the texture of the skin by their presence. They may be single or grouped and small or large. They may disappear after a few months, perhaps as a result of being hidden by deeper pigmentation of the surrounding normal skin, as noted by Metzger and Clarin (Bull. Soc. d obst. 23 44., 1934) Ashmead (JCutD 23 203 1905) considered them a primitive simian characte Their presence seems not to have factual relationship with mixture of racial blood, although the lesions are commoner in Mongolian and Negro d races than in the white (Edit. J 115: 2182, 1940) The pigmented cells represent accumulations of dopa positive cells of the corium, which, f extremely densely overgrown, comprise the blue nevus (q.v.); see Ahmed (AfDuS 141: 171 1922) Piers (EAfrMJ 23 10, 1946)



Fig. 728 —Lentigines, forea m nd arm



Figs 729 and 730 —Chloasma, which developed soon after influenza.

**Etiology and Pathology** —Autochthonous pigmentations of the skin are of two general classes hemosideroses (iron-containing see also hemochromatosis and Schamberg s disease) and melanoses (iron free see lipomelanic reticulosis and ochronosis) Freckles and lentigines belong in the latter group Deposits of pigment are found in the lowermost epithelial cells. The basal layer contains two types of cells the epithelial which may hold pigment granules, and the melanoblastic dendritic elements, which elaborate it Pigmented nevi may be elevated with their content of nevus cells or they may be macular, consisting only of an abnormal number of melanoblasts Macular melanomas are to be li-

tinguished from freckles. Pigmentation may also be due to deposits of metals (argyria) or to extraneous materials (tattoo). See Becker (ADS 16: 259 1927 Clinics 3 896, 1944 JInvD 7 381 1946, comparative anatomy)



Figs 731 and 733.—Tattoo, decorati[illegible] and histologic lesion, showing pigment granules in dermis and no inflammation (Dr George H. Belote.)



Fig. 73[illegible] Fig. 73[illegible]

Fig. 73[illegible]—[illegible] [illegible] from use of [illegible] on [illegible]. (Sutton [illegible] 112 [illegible] 193[illegible].)

Fig. 7[illegible] [illegible] of [illegible] (Dr F Ronchese.)

Pigment [illegible] [illegible] the [illegible] action [illegible] heat pressure [illegible] action from [illegible] [illegible] scratching provoked by pruritic disorders, actinic light [illegible] [illegible] [illegible] and chemical irritant. Brunets are able to produce [illegible] [illegible] [illegible] the skin. [illegible] and Negroes most inflammatory [illegible] [illegible] [illegible] local production of pigment. The lesions

of pityriasis rosea, furuncles, erythema multiforme drug eruptions, pellagra, lichen planus, acne and the like do this. Months may pass before normal coloration is regained. Some inflammatory lesions such as lupus erythematosus and achromia parasitaria lead to depigmentation.

Internally caused, the lesions may develop during the course of certain constitutional disorders, generally hypoendocrine affecting the thyroid, gonads, or adrenals. Pigmentation is a characteristic of acanthosis nigricans (p. 409) and is sometimes seen in various chronic debilitating diseases such as tuberculosis, starvation, malaria, secondary syphilis, cirrhosis of the liver and cancer (Brunsting MCNAm 21: 801, 1937). In pregnancy pigmentation is increased over the whole body, the nipples and areolae, linea alba, pudendal regions and flexures being sites of greatest increase. Several varieties of dermatitis medicamentosa are associated with pigmentary changes: fixed eruptions, arsenical pigmentation (diffuse as from small drops of rain). Atabrine, gold, silver (argyria) see p. 100. Administration of estrogen sometimes induces pigmentation, sometimes cures it (Rosen: JClEndocr 2: 317 1942)

**Tar Melanosis.**—Brown violet, reticulated discoloration of the uncovered areas of workers with certain tars has been observed, a form of contact photosensitization (Foerster and Schwartz ADS 39: 55, 1939). Brown patches develop on the exposed skin of workers handling tarry materials, accompanied by slight hyperkeratosis, scaling and follicular keratosis, as reported by Riehl. The onset is gradual, often with some erythema. The lesions once formed are persistent. The mucosae are not involved. Kinnear's patient was photosensitized by oil in jute spinning. Pitch dermatitis and melanosis were studied by Foerster and Schwartz (ADS 39: 69 1939) who concluded that acridine and anthracene are not the sole agent inciting pigmentation, and that tar melanosis is true contact photosensitization (p. 89) due to light of 3,900 to 5,000 A.U. Meadow grass dermatitis leads to similar melanin deposition. See Rudloff et al (abs BJD 58 256 1946): some cases clear on thyroid; familial cases; cosmetics and impure paraffin as etiologic factors; relation to lichen planus, avitaminosis C, nervous tension. Occupational melanoderma was reviewed by Schwartz (ADS 56 592, 1947)

Poikiloderma of Civatte is probably the same as Riehl's melanosis (Kinnear: BJD 47 101 1935). It is characterized by pigmented and atrophic macular lesions occurring in a network of irregular patches symmetrically on the face and neck. The patches are reddish brown and are surmounted by fine small, white, adherent scales. The patients are usually women of menopausal age.

**Erythrose Pigmentaire Péribuccale.**—Diffuse brownish red pigmentation about the mouth and chin, even including the forehead, with or without slight burning sensations, is seen in women of middle age. Much of the color disappears on diascopy. The disease is rare but clinically distinctive. It is probably related to female hormonal influences, but is unresponsive to any known therapeutic measure. The patient usually is in abundant health and complains only of the disfigurement (Ormsby and Ebert: ADS 23 429 1931). Cohen (BJD 60 403, 1949) gave a thorough review and suggested the administration of thyroid and estrogen.

**Hypophyseal Cachexia; Simmonds Disease.**—Emaciation, amenorrhea, hypogenitalism, hypotension, hypoglycemia, low basal metabolic rate, asthenia, dental caries, atrophy of the mandible and generalized pigmentation are characteristic features (Wilson BMJ 1 814 1936). Weakness, loss of normal hair, increase of hair on the face, slow pulse, and anemia are also observed. Little response to opotherapy may be obtained. The patients seem to undergo speedy senility and they die.

**Felty's Syndrome** comprises chronic deforming arthritis, splenomegaly, lymphadenopathy, leucopenia and cutaneous pigmentation, dusky nodules, and subfebrile temperature (Felty B JHH 35 16 1924; De Gennes et al. Presse méd 44 377 1936). Singer and Levy (AIntM 5 576 1936) considered it the adult form of Still's disease, a sepsis lenta, perhaps due to *Streptococcus viridans*. A case of Still Chauffard disease was seen in a boy of 14 years, in whom it began at the age of years with arthritic symptoms involving the extremities and cervical spine; the cheeks were especially pigmented.

**Osteodystrophia Fibrosa.**—See p. 390.

**Treatment.**—As in all disorders of obscure origin the patient must receive thorough general examination. Remedies to be advised depend on the result of such an investigation. Thyroxin when needed works well. Pigmented patches can sometimes be temporarily removed by the



Fig. 35.



Fig. 736.



Fig. 737

Fig. 735.—Depigmentation secondary to chronic lichenoid dermatitis of leg. (Dr O. G. Costa.)

Fig. 736.—Vitiligo.

Fig. 737.—Vitilig extend e, in Negr woman.

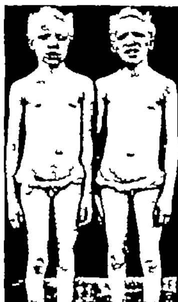


Fig 738

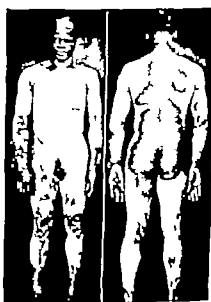


Fig 739

Fig. 738.—N gro, lbino uniovula twins (Wakefield nd Dillinger AJ tM 9 1149 1936.)

Fig. 739.—Pi bald albi ism "The Leopard M n. A heredit ry lomina t pig mentary anomaly (Ka ler J 103 179 1934.)

**Connective Achromia** is the symptomatic loss of pigment resulting from such dermatoses as tinea versicolor syphilis, pinta, psoriasis, neurodermatitis, l pus erythematosus and leprosy The vitiliginous lepral is not completely achromic, and the lesions are thermoanalgesic.

The skins of some Negro workers were bleached without inflammation by the hydroquinone antioxidant of their rubber gloves (Oliver et al.: J 113: [illegible] 1939; Schwartz et al. PHRpts 55 1111 1940) Hairs were not depigmented. Repigmentation eventually followed withdrawal from contact with the chemical, Agerite alba.

**Pseudoachromia Parasitica** is characterized by actinic hyperpigmentation of normal skin about the more or less circular macules of tinea versicolor The areas of



Fig. 740.—Vitiligoid nevus unius lateris no textural change.

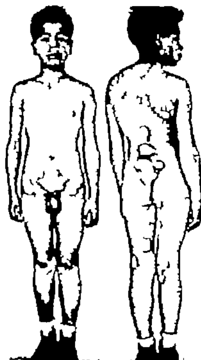


Fig. 741.



Fig. 742.

Fig. 741.—Vitiligo. (Dr [illegible] Schrade.)
Fig. 742.—Incontinenti pigmenti (Hopkins and Machacek: ADS 43 [illegible] 1941.)

infection are pale because the fungus is relatively opaque, though the sunburn which hyperpigments the normal skin may desquamate and cure the disease. See achromia parasitica, p. 321 and Fig 390 on p. 320.

**Albinism** is congenital achromia. It may be partial or universal. In partial albinism, the lesions simulate those of vitiligo but hyperpigmented areolae are not present. Rarely the lesions may be distributed as in nevus unius lateralis. Hair in involved areas is white.

In universal albinism the absence of melanin is complete. The pupil of the eye appears red and the iris pink or bluish from reflected light, and there are present more or less astigmatism, photophobia and nystagmus. The hair is white or pale yellow and is silky in texture. The skin is whitish or pinkish in color and cannot tan on exposure to sunlight. Inheritance of the anomaly as a Mendelian recessive is often noted. With the exception of the absence of pigment, the skin is normal in every respect.

**White Forelock** occasionally occurs as a sort of partial albinism, sometimes alone, when it may be inherited as a dominant character and sometimes as the scalp manifestation of piebald albinism (Nussey Lancet 2: 947 1933) See p. 663 also Fig 990.

**Incontinentia Pigmenti** is the name Sulzberger (ADS 38: 57 1938) preferred for 8 remarkable cases showing bizarre, macular irregularly shaped and disseminated areas of tan pigmentation, jagged and sharp in outline not zosteriform, not definitely systematized, involving the trunk and extremities The onset was at an early age, the lesions perhaps being present at birth. In the epidermis he noted only slight changes, but in the cutis were large numbers of coarse, dark granules of melanin in the connective tissue chromatophores. The dopa reaction in the cutis was negative, and no formation of pigment was there demonstrable This distinguished the lesions from those of blue nevus or Mongolian spots. The picture suggested autochthonous tattooing, as though the epidermis had become incontinent of its own pigment and had let this descend into the cutis. Naegeli's cases were familiar Sulzberger's case was unilateral in distribution, associated with ectodermal defects which were familial. The patient of Hopkins and Machacek (ADS 43 728, 1941) was a Negress.

## TATTOO AND POWDER STAINS

**Tattooing** consists of introducing insoluble substances such as carmine, cinnabar indigo and carbon into the dermis. Infection with syphilis, tuberculosis, verrucae and other diseases may result from the use of dirty tattooing needles The coloring matter rests within the connective tissues surrounded by a fixed tissue foreign body reaction (Bettley BJD 52 129 1940) and without being removed by phagocytosis, so that it is indelible permanent, and removable only by procedures which scar Accidental tattooing is seen in powder burns, excoriations and lacerations which introduce carbon into the skin. The miner and the soldier are occupationally subject to this.

**Methods of Removal** are of 3 types surgical electrolytic, and chemical. Long narrow marks may be excised. The superficial layers may be shaved off by means of the dermatome, and the area may or may not require covering by grafting Minute specks of powder stains can be removed by the negative galvanic needle or dug out by a small sharp curet. They should be removed at the earliest possible moment, and this can be done by scrubbing the skin immediately after its injury with a sterile brush. An effort can be made to hide unsightly powder marks by tattooing flesh-colored pigment over them. One can protect the border with petrolatum, moisten the skin with strong tannic acid solution needle the design, rub it with silver nitrate stick, cover it with powdered tannin and await the slough (Shie J 90 90 1928 Bettley BJD 52 129 1940 Bloom ADS 41 619 1940 electrodesiccation)

As an adjunct to plastic surgery tattoo may be used to improve the color of a graft to simulate beard stubble or eyebrows (Matthews Proc RoySocM 40 881 1947) or to hide a birthmark (Conway and Doktor: SGO 84 866, 1947)

Foreign body reaction in the form of a benign tumor may result from tattooing (Madden ADS 40 256, 1939) Sensitization to the mercurial pigment has been reported (Madden ADS 38 481, 1938 MacDonald J 114 1481, 1940)

Iron Deposits in the Cutis sometimes result from the application of an iron salt, usually copperas, to an exudative dermatitis. The brown stain is presumably a basic ferrous acetate or similar organic combination attached to the collagen in a relatively permanent way (Sutton: J 108: 112, 1937) The tattoo accurately outlines the previously exudative areas with sharp margination, and it is generally a bit deeper in color at the periphery Sometimes the discoloration can be removed by ultraviolet or cantharides blistering. It disappears spontaneously after a few years. Iron salts have been applied far more often than they have caused pigmentation. It seems that the mordant action of a weak organic acid is simultaneously requisite (QMN J 114 431, 1940 Strauss: ADS 53: 602, 1947)

Rust, or the carbon from flaming the needle may tattoo the morphine addict (Wright and Friedman ADS 40: 630 1939)

## CAPITULATION OF PIGMENTATIONS

Practically every hyperpigmentation will fall within this list

**Physical and Chemical Agents**
- Sunlight
- X-ray radium
- Radiant heat
- Cold
- Friction
- Contact photosensitization
- Photodynamic sensitization
- Tattoo
- Medicinal arsenic, bismuth, mercury lead, silver copper gold, atabrine, phenolphthalein, picric acid, TNT dinitrophenol

**Systemic Conditions**
- Addison disease acanthosis nigricans
- Avitaminoses
- Hemochromatosis
- Ochronosis
- Lymphoblastomas
- Polycythemia
- Malignant melanoma
- Chronic debilitating diseases
- Xanthoma
- Carotinemia
- Urticaria pigmentosa
- Jaundice
- Pernicious anemia
- Scleroderma
- Familial anomalies incontinentia pigmenti osteodystrophia fibrosa

**Endocrine Conditions**
- Pregnancy
- Estrogen overdosage
- Menopausal abnormality
- Thyroid dysfunction
- Chloasma
- Pituitary basophilism
- Adrenal cortex tumors
- Bronze diabetes
- Mongolism

**Disturbances Involving Skin Directly**
- Ephelis
  - Recklinghausen's disease
- Mongolian spot
- Lentigo
- Pigmentary nevus
- Seborrheic keratoses
- Darier's disease
- Xeroderma pigmentosum
- Parasitic infestations, pediculosis
- Tinea versicolor
- Chronic inflammations
- Lichenification, dermatitis venenata, dermatitis herpetiformis, lichen planus, varicose dermatitis, exfoliative dermatitis, syphilis, pinta, tuberculosis, pruritus, erythema multiforme
- Purpura, Schamberg's disease, Majocchi's disease poikiloderma, stasis dermatitis


Albrecht CurMDig, Aug. 1948, p. 17
Armstrong MCNAm 21 881, 1937 (systemic diseases)
Goldsmith CMAJ 67 397 1932.
Hollander and Baer ADS 20 37 1929.
Edit. J 126 734 1944 (estrogens)
Montgomery J Lancet 64 472, 1939
Edwards and Duntley AmJ Anat 65 1 1939 (spectrophotometric study)
Jeghers NEngJM 231 88, 122, 181, 1944 (complete review)

Types of atrophy have been classed (Sweitzer and Laymon ADS 31 196 1935) as those present at birth and those which are acquired, the latter being divided into those associated with inflammation and those not associated with inflammation

**Congenital Atrophies** (malformations, q.v.)
- Congenital ectodermal defects (q.v.)
- Congenital nevoid atrophy
- Diffuse universal atrophy

**Acquired Atrophies**
- NONINFLAMMATORY
  - Senile
  - Externally influenced
    - Degenerative senile (see keratoses)
    - Xeroderma pigmentosum (q.v.)
    - Roentgen and radium atrophy (q.v.)
    - Atrophic striae striae distensae
    - Pressure and occupational atrophy
  - Internally influenced
    - Hunger marasmus, cachexia
    - Nervous and trophic influences
- INFLAMMATORY
  - *Progressive chronic atrophic dermatitis*
  - Diffuse atrophic dermatitis
  - Acrodermatitis atrophicans
    - Macula atrophicae dermatitis (primary macular atrophy)
    - Poikiloderma
  - Blepharochalasis
  - Kraurosis
  - Atrophy consequent to scarring inflammatory diseases (secondary macular atrophy) lupus erythematosus syphilis, leprosy tuberculosis, lichen planus, lichen sclerosus et atrophicus, scleroderma, morphea, pellagra

**Diffuse Idiopathic Atrophy of the Skin.**—Atrophy in these cases is probably not primary atrophy but rather dermatitis passing into atrophy Many cases once classed among idiopathic atrophies can nowadays be recognized as symptomatic

**Acrodermatitis Chronica Atrophicans** is a descripti e term, according to Sweitzer and Laymon (ADS 31 196, 1935) who stated that Oppenheim limited thi name t cases haracterized by (1) doughy infiltration at the onset (2) the presence f ulnar bands, (3) the *localization on the extensor surfaces of th* extremities, especially the knee elbow and finger joints and (4) the absence of vol ement f the entire body The face nd the palms and soles are not invol ed and the trunk almost never Fibrous nodules ma occur ppearing painlessly in the subcutaneous tissue over the extensor surfaces by predilection, on the lbow knees, and wrists, but to pea size singly or i groups. Scleroderma like ha ges occur in about one-th rd of the cases, most ften on the lower part f the leg and dorsum of the feet The glazed colorated areas may ul cerate Some ses re associated w th rthrit deforma and atrophy of the bone No etiologic feature has been determined although *absorption f* *tsetse spray* may have been ignified t cases f Breuckmann (YBD 1940 p. 167)

Acrodermat tis hronica atrophicans i t be differentiated from scleroderma, particularly scleroderma f the edematous type Some cases f acrodermatitis hronica atrophicans ca not be d fferentiated from the edematous f rm of scleroderma at any stage The general health sually little affected The progress of the disease is gra

erally slow but progressive fo a time after which it remains relatively stationary. The changes are permanent.

Therapy is symptomatic and palliative. Warm baths galvanism, and massage have been recommended. Various endocrine and vitamin preparations appear to be worthless here. Elimination of focal infection affords someth ng to do.

Interesting cases exemplifying various types were presented by Schmitt et al. (ADS 40: 674, 1939). Familial incidence the patients being si ters, was noted by Director and Bluefarb (ADS 46 490 194.). The ntire skin became involved in Graham patient (ADS 50 253, 1944). Montgomery and Sullivan (ADS 51: 32, 1943) reviewed 43 Mayo Clinic Cases of acrodermatitis chronica atrophicans stressing histologic studies.

**Glossy Skin.**—The sites of predilection of neuritic atrophy are the extremities. The affected skin is at first reddish or purplish, becoming grayish, glossy and shining so as t resemble an atrophic scar. Fissuring and ulceration are likely t occur and the cutaneous appendages undergo atrophy. Reflex dystrophy of the extremities was reviewed by de Takats (AMArg 34: 939 1937). Vasomotor phenomena are prominent at first, but are later overshadowed by trophic symptoms. Hard, nonpitting edema is usually present. The edema is accompanied by paroxysmal pain, sensitivity to tempera ture hanges and especial tenderness on pressure. There may be considerable sweat ing. The nails become brittle and ridged. The skin becomes glossy and bluish, and is the site of eczematoid eruptions. Eventually there develop contract res and shrinkage



Fig 712.—Acrodermatitis chronica atrophicans associated with arthritis deformans. Sweitzer and Laymon ADS 31 196, 1935.)

of the joint capsules. Some cases ar helped by interference with the sympathetic innervation. Cervical ribs ma cause trophic changes. The disease is secondary t neuritis, and the neural lesion may follow gun-hot wound disease f the cord vascula disease (Pettersson and Sjöqvist J 114 2273, 1940) or some const tutional disorder such as gout or rheumatism. All f de T kat cases followed such lesions as might damage the blood supply to the sciatic nerv. K rasch (JNervMentDis 84 ... 1936) demonstrated cases in which the evidence w clear that the cause of the change was damage f the vascula supply t the nerves. Causalgia is with few exceptions, he pointed out the peculia property f the median nerv the t bial portion of the sciatic nerve and t a lesser extent the ulna nerve. The outlook is not good, and pain is diffi ult t allay. Tonics, particularl frams B, arsenic an I iron, may be in dicated. The limb should be kept w rm, and prec utions taken to guard against sud den changes f temperature.

## MACULAR ATROPHIES

**Anetoderma of Jadassohn** begins with l ttle circumscribed, erythematous macules which fade at the center and form circular lesions w thin which atrophy progresses. The surface becomes shiny whit and crinkly and the central region may protrude baglike with redd sh or ellowish coloration (Andrews *Dis of Skin*, Saunders, 1946).

This variety of primary macular atrophy has an initial erythematous stage (Oppenheim and Cohen: ADS 50 64 1944) Endocrine therapy may influence its progress which is reminiscent of localized myxedema, in an occasional case like that of Foerster (ADS 34: 725 1936) whose patient manifested Frolich s syndrome.



Fig. 744—Multiple benign tumorlike new growths (Schweninger-Buzzi disease) (Sweitzer ADS 6: 599 1922)



Fig. 745.



Fig. 746.

Fig 45—M la troph due t syphilid. (Dr A. Loveman.)
Fig. 46—M phus, trophic, en coup d sabre (Dr James A. Mitchell.)

**Multiple Benign Tumorlike New Growths of the Skin.**—The Schweninger Buzzi type of anetoderma is characterized by the occurrence of small, soft bean to pea size circumscribed, wh t h or bluish whit bladderlike f rmations, many of which can be pressed into a hollow in the underlying tissue, like small hernias. The shoulders, arms, and dorsal surface f the trunk are the regions commonly invol ed. The lesions develop slowly with associated cutaneous atrophy There are no symptoms. This type of

atrophy is a clinical entity according to Chargin and Silver (ADS 24: 614, 1931). Pusey (JCutD 35: 582, 1917) whose patient's face and back were affected, found a dearth of elastic fibers suggestive to him, of congenital defect. The disorder is a rare form of primary macular atrophy for which therapy is unavailing. See Butterworth (ADS 29: 891 1934) Tobias (ib., p. 210) Kampf (ib. 33: 116, 1936).

**Secondary (Macular) Atrophy** is the result of destruction of the elastic tissue by inflammatory infiltration, however diverse the causes of this may be (Scull and Nomland ADS 36: 809 1937) Syphilis is a common cause. Elastic tissue destruction may result from subclinical inflammation. Xanthoma tuberosum on resorption may leave atrophic residuals (Hubler ADS 50 211, 1944).

Red plaques of 1 to 5 cm. diameter located mainly on the extremities of a hypo estrogenic female healed during her pregnancy and later spectacularly abated under stilbestrol therapy leaving atrophic scars (Sweitzer and Winer: ADS 54: 481, 1946).

White spot disease is subdivided nowadays among atrophic morphea, lichen planus, lichen sclerosus, and macular atrophy (Ormsby ADS 40: 133 1939).

## FOLLICULITIS ULERYTHEMATOSA RETICULATA

MacKee and Parounagian (JCutD 36 33 601, 1918) described a symmetric eruption limited to the cheeks, occurring in young persons, and consisting of numerous, closely crowded, small areas of atrophy separated by narrow ridges. This produces a reticulated honeycomb or network appearance. The individual atrophic areas are pitlike abrupt, and about 1 mm. in depth, and they range from 0.25 to 2 sq. mm. across. In places, two or more depressions may unite to form areas perhaps 3 sq. mm., or even larger. There are a few small comedones, both in the depressed areas and in

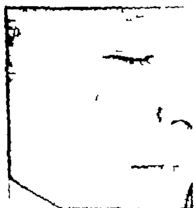


Fig. 747



Fig. 748.

Fig. 747.—Folliculitis ulerythematosa reticulata.
Fig. 748.—Blepharochalasis. (Benedict J 87 1726, 1926.)

the ridges. A number of milium bodies are sometimes noted in the ridges. The skin covering the narrow partitions or ridges is on a level with that covering the unaffected portion of the face. The skin seems somewhat waxy, stretched more resistant, harder than the normal skin. The entire affected area may be irregularly erythematous. See MacKee and Cipollaro (ADS 5 231 1945).

Ulerythema Acneiforme is similar being characterized by symmetric erythema of the cheeks with follicular comedo like lesions which lead to peculiar netlike scarring. The disease may exist with or without notable inflammation. It begins in early youth and commonly has undergone its complete evolution, with permanent scarring, before middle age.

**Atrophoderma Reticulatum** is an inclusive title for such disorders (Winer ADS 34 941 1936), for which there are several synonyms, such as honeycomb atrophy (Sa atard BJD 55 239 1943) The cause is unknown. These conditions differ from linear comedo nevus and grouped comedones, although symmetrically grouped comedones with atrophy and resorption instead of foreign body reaction and acneform pustulation would produce an identical picture There may exist in etiology an important element of hypothyroidism and possibly of avitaminosis. Difference from acneic scarring is discernible, however and MacKee's disease appears in early childhood No known method of treatment is helpful.





Figs. 749 and 750.—Hemiatrophy of face of a girl of 13 years roentgenogram revealed intracranial calcification (Merritt et al, JPed 10 374, 1937)

## PSEUDOATROPHODERMA COLLI

This is a rare pseudoatrophic disturbance of the skin of the neck, which was observed by Becker and Muir (ADS 29 52, 1934) in 2 otherwise healthy young women. The lesions were depigmented, macular and somewhat glossy and over them the epidermis was thrown up in tiny folds. The delicate wrinkling was eradicated temporarily by stretching the skin. Between the shiny macules the skin was dull and slightly scaly but textural difference was lacking Microscopathologic change was slight. The cases of Frost and Epstein (ADS 40 753, 1939) in sisters, were parapsoriasiform. The back, chest, and arms exhibited the disorder in the woman reported by Ayres (ADS 52 280 1945) The cause and treatment are unknown, though it may be a female endocrinologic disorder on which one might try an estrogenic cream.

## ATROPHIC STRIAE (STRIAE DISTENSAE)

These symptomatically follow mechanical overstrain as in pregnancy (lineae gravidarum) tumors, obesity and ascites There is also a type which is apparently idiopathic, but the possibility that the lesions have been caused by either trauma or overextension can seldom be excluded. A common site is the lumbar region of young people (*Rosenthal Lancet 1 557 1937*) *The thighs and breasts are often affected.* Weight gain as well as weight loss may occasion their development. Nothing can be done about them. The lines are transverse, red at first becoming white and slightly sunken, and are completely asymptomatic. Astonishing striae may be seen in basophile adenoma of the pituitary gland (Cushing J 99 281 1932; Hall et al.: Lancet 1: 882 1939)

## HEMIATROPHY

Hemiatrophy may include the entire half of the body—some 23 cases of total hemiatrophy have been recorded—and it may include more than the fifth nerve distribution. Fifth nerve distribution is, however, usual. Tauber and Goldman (ADS 39: 606 1939) said that more than 400 cases of various stages of progressive hemiatrophy had been published. Histologic changes of the skin are meager but the scalp regions affected show alopecia. Hemiatrophy of the face is a rare striking abnormality usually of early onset, without predilection as to sex, with involvement of all structures of the affected side, although the skin may escape. The muscles do not lose their function, but the subcutaneous fat is greatly diminished, and the bones themselves are actually smaller. Archambault and Fromm (ANeurP 27: 529 1932) reported that the atrophic process may begin at any point about the orbit, angle of the mouth, nose or malar area; it spreads gradually or rapidly over the entire half of the face. It may come to a standstill at any stage. Falling or blanching of the hair in affected areas is common. Abnormal pallor is usual, and this may signify that the vessels are atrophic. Neuralgic pains frequently accompany the atrophy; they may precede its onset or may occur during its course; they are associated especially with atrophy in the trigeminal area. The cause is unknown. No treatment can be offered excepting perhaps sympathectomy or plastic surgery (Kazanjian and Sturgis: J 115: 349 1940).

## BLEPHAROCHALASIS (ATONIC PTOSIS)

This is a disease of the upper eyelids which is characterized by permanent swelling of the lids, with great thinning of the skin and bagginess of the lids. As a rule, the involvement is bilateral.

Benedict (J 87: 1735 1926) wrote: "The disease is usually found in young persons as an intermittent swelling of the upper lids. It makes its appearance soon after puberty as a transient edema of the upper lids lasting for a few hours, the attacks coming on at intervals of a few days or a few weeks. Succeeding attacks last longer and appear more frequently, until permanent swelling of the lid with great thinning of the skin and bagginess of the lids results. The bagginess and atrophy of the skin are the characteristics of the disease by which the name blepharochalasis is suggested. The onset is usually insidious, and its early manifestations are overlooked or misinterpreted. The diagnosis becomes clear only after permanent changes are brought about in the lids. The disease is more commonly found in young girls but has been observed in young boys and even in old men. Fuchs observed it in the lids of a man past middle life. It has been recognized in later life in persons who have had the swelling of the lid and atrophic appearance of the skin since early youth. Blepharochalasis is to be found in 2 stages. The first is the intumescent state or stage of edema. The early attacks of swelling resemble those of angioneurotic edema and last, usually for from 2 to 4 days, without pain, and with only slight redness of the skin. After several attacks of swelling, one of two things occurs: (1) The swelling becomes constant with bagginess of the skin of the lid so that loose folds hang down over the margin, giving the appearance of water-filled bags, with the skin altered slightly in color, very thin and slightly folded or wrinkled; or (2) the swelling disappears entirely or occurs for only short times, at intervals of weeks or months, and the skin becomes reddish brown and wrinkled, and is thrown into horizontal folds resembling brown wrinkled cigaret paper. The latter condition causes less interference with vision but may be accompanied by true ptosis, as shown by the first case of this series. The stage of wrinkling is the end stage of the disease."

*The cause may be* cutaneous *dermatitis with secondary atrophy.* *Plastic surgery* may be used. It may require repetition if attacks are still occurring.

## POIKILODERMA ATROPHICANS VASCULARE (JACOBI)

This is a rare dermatosis of slow evolution, characterized in the early stages by the appearance of extensive but discrete areas of skin with fading margins, within which occur pruritus of varying degree, telangiectases and pigmentation, followed by capillary hemorrhages and atrophy similar to that induced by roentgen radiation (Lane: ADS 4: 563, 1921; 15: 621 1927).

The term "poikiloderma" has been confused by indiscriminate inclusion within its meaning of atrophies now classified otherwise, and poikiloderma of Civatte is identical with, and is described under the title of, Riehl's melanosis (Kenney: BJD 47: 191, 1935).



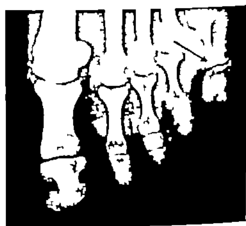
Fig. 751.



Fig. 752.

Fig. 751.—Poikiloderma atrophicans vasculare (Hazel ADS 40 776, 1939)
Fig. 752.—Poikiloderma atrophicans vasculare. (Lane ADS 4 563 1921; 8 373, 1923)





Figs. 753 and 754.—Ainhum lesion of fifth toe of Negro, and roentgenogram showing atrophy of phalanges. (Spinzig AmJR 42 246, 1939)

A case which eventuated in mycosis fungoides was carefully described by Oliver (ADS 33: 767, 1936) and this is the usual outcome, according to Hazel (ADS 40 776, 1939). The patient of Smith (BJD 52 218 1940) showed enlargement of the liver and spleen and had 8 per cent monocytes and 45 per cent large lymphocytes in the blood. Differential diagnosis from dermatomyositis (q.v.) was clarified by Dowling and Freudenthal (BJD 50: 519 1938). See Downing et al. (ADS 56: 740 1947) who noted that some cases do not develop mycosis fungoides.

In treatment, grenz rays helped a patient of Dostrovsky and Sagher (ADS 51 152, 1945) and x rays should be about as useful as in mycosis fungoides (q.v.). A patient who also had syphilis was apparently cured of both diseases by arsenicals and fever Kalz and Hoogstraten (ADS 53 532 1946) reported.

## AINHUM

Ainhum is a disease affecting the pedal digits. It is characterized by the development of a callused groove which constricts, strangulates and leads ultimately to spontaneous amputation within 3 to 10 years of the toe distal to the groove. Cases are occasionally observed in the United States, but the disease is essentially a tropical one. The vast majority of its victims are Negroes. Ulceration occasionally develops at the site of the encircling band; this results in some pain, which is otherwise inconsequential. While the separation commonly occurs at the first or second phalangeal joint, it may take place in the continuity of the phalanx. Fingers as well as toes are sometimes attacked by encircling amputating bands resembling ainhum (Bluefarb ADS 57 741 1948).

The cause is uncertain. The name ainhum should not include all cases of digital amputation, even if the term is limited only to amputations associated with encircling bands. Lepra, scleroderma, cicatrix, and atypical forms of keratoderma have all caused spontaneous amputation. A boy we examined (ADS 38 76, 1938) whose mother was similarly affected, had abnormally short terminal phalanges of the great toes, and absence of the terminal cancellous tufts. This resulted in weight bearing on the crease beneath the interphalangeal joint instead of on the pads of the toes, and so led to the production of grooved calluses. The bending of a digit at the site of a grooved callus is the analogue of bending a paper tube, bending a tube occludes the hole through it. Histologic findings give no clue to the cause (Keen and Tucker APath 41 639 1946). Roentgen findings were given by Spinzig (AmJR 42 246 1939).

Therapeutic incisions of the constricting band do not succeed. Amputation is usually indicated, after which pain disappears and the stump heals promptly. See Vaughn et al. (AnnSurg 122 868 1945).

## SENILE ATROPHY

Senile changes in the skin usually develop slowly and consist of loss of subcutaneous fat and thinning of both dermis and epidermis. Manifestations of atrophy are seldom pronounced before the fiftieth year but they may develop early. The skin becomes yellowish, thin, harsh and inelastic, and is frequently the seat of brownish or blackish pigmented macules, some of which develop into keratoses. The changes are usually most marked on exposed parts, the face, neck, dorsa of the hands, and the legs. Occasionally the affected skin instead of being dry, rough, and harsh, is soft, pliable, shiny and marked by whitish, atrophic spots or streaks. The hair follicles are affected, and the dermal papillae are flattened. Histologically the elastic tissues show the most marked changes (Hill and Montgomery JInvD 3: 231 1940). Itching is a frequent symptom, especially in winter when the humidity is low and the skin is dry and harsh. The condition can be ameliorated by the use of simple emollient applications and the avoidance of excess of sunshine, hot water and soaps. Some skins tolerate cool water when hot water provokes itching. Vitamin A and estrogenic or androgenic substances may help.

## KRAUROSIS

Kraurosis is a progressive sclerosing atrophy of the mucocutaneous teguments of the vulva which leads gradually to stenosis of the vaginal orifice, to disappearance of the labia minora prepuce and clitoris, and to effacement of the labia majora (Montgomery et al ADS 30 60 1934) The mucosa becomes smooth shiny and dry the color is white waxy yellow or spotted and complication by leucoplakia is frequent so that the development of carcinoma is likely The underlying pathologic basis is thought to be suppression of ovarian function by senile involution, sclerosis, or castration. Kraurosis is not to be confused with inflammatory leukoplakia, lichen planus, lichen sclerosus, neoplastic leucoplakia, or the lichenification which results from chronic pruritus from contactants or parasites. Yet there is considerable similarity between vulvar lesions of kraurosis, mucosal lesions of avitaminosis A the Plummer Vinson syndrome (q v ) and lichen sclerosus, the chronic, progressive, atrophic, sclerotic process which often affects the vulva or the glans and prepuce of the male as balanitis xerotica obliterans (Freeman and Laymon ADS 44 547 1941)

Kraurosis is a shriveling disease of later life, progressive until carcinoma develops eventually and associated with severe itching as a rule Some authors, recognizing the condition as precancerous, advise vulvectomy at an early stage. Vulvectomy generally becomes necessary (Sparrow AnnSurg 112 87 1940) although many reports of the efficiency of estrogenic hormonal substances have given encouragement in this distressing disease (Foss JObGBF 46 271 1939 Buxton and Engle J 113 2318, 1939) Estrogen may help the atrophy without relieving the itching so that resort to surgery may still be required.

Kraurosis of the penis is described (Beck DeGregorio et al. abs YBD 1939 p 263 264) wherein symptoms and mucosal alterations are analogous to those occurring in the female.

*Stilbestrol, 20 mg to the ounce of petrolatum* applied locally apparently cured one patient (Feldman ADS 43 756 1941) Hydrochloric acid, vitamin B complex, and iron may be given by mouth. Administration of vitamin A and, if hypochlorhydria is present, HCl may be helpful (Swift JObGBE 43 1053 1936) Roentgen therapy may afford temporary relief. Bland antipruritic lotions and packs may be used. The avoidance of contactant irritants is advised. See Saville (BJD 52 338, 1940) and Hunt (Diseases Affecting the Vulva Mosby 1948) Estrogen in suitable dosage when given intramuscularly may yield greater benefit than when given by mouth or applied locally

# DERMAL MANIFESTATIONS OF MALFORMATION AND NEOPLASIA

**Growth Disturbances** characterize neoplasia, the subject matter of this chapter and embryology appears the key to these. Aberrations of form and function comprise the benign and malignant tumors which may be interpreted as manifestations of one process. The modern concepts of organization induction and abnormalities of these processes represent clarifications of ideas held by wise old observers such as Cohnheim who spoke of "versprengte Keime" (sprung up embryos) and Albrecht, who coined "hamartoma" (error tumor). See Harvey (EdinMJ 55: 1, 1948). The range of variation among tumors seems almost endless, but appears to be governed by the number and variety of tissues involved in the anomaly and the genetic or mutational potentialities of the cells of which they are composed. Abnormalities may be localized or systematized in distribution. Some varieties are common while others are rare and still others almost unique.

## ICHTHYOSIS

Ichthyosis is a congenital abnormality characterized by cutaneous dryness, harshness, and scaliness manifestations of irregular hypercornification. It is a fairly common condition. The disorder is usually solely cutaneous and ranges considerably in distribution and degree of severity. The general health is unaffected. Extensor surfaces of the limbs are the sites of predilection, although the entire body may be involved. During warm months when the skin is moist and better lubricated, the lesions in mild cases are scarcely perceptible, but the disorder becomes conspicuous in the low humidity and cold of winter. Some patients, lacking the ability to perspire carry a slight fever in the summer and their fatigability and tremor suggest hyperthyroidism. They are especially vulnerable to irritation by soap and to pruritus consequent on dryness. The face escapes involvement except in severe cases in which are seen dry scaliness, tautness, eyelid changes and ectropion with glazing of the conjunctiva and danger to the cornea (Cordes and Hogan AOphth 22: 590, 1939). Rarely the cornea is affected by its participation in the epidermal defect (Vail AOphth 24: 215, 1940).

These cases resemble avitaminosis A and myxedema, but are not responsive to the vitamin (Peck et al. ADS 48: 32, 1943) or to thyroxin. Locally frequent inunction with a bland ointment, such as cocoa butter or benzoinated lard, is somewhat comforting. One per cent salicylic acid can be added to advantage. These applications act best when applied immediately following a hot bath in soft water. Gordon (ADS 52: 178, 1945) reported benefit by the use of Ljungstrom's daily baths in 3 per cent NaCl followed by inunctions of 10 per cent NaCl in hydrous wool fat, giving also vitamin A and, to enhance its utilization, bile salts and neostigmine. No illusions should be entertained regarding the value of drugstore shelves, some items of which are almost certain to irritate. The patient has to learn to live with his defective skin.

Inheritance is variable, being sometimes dominant, sometimes sex linked (Davies and McGregor BJD 54: 121, 1942) or the disorder may

appear as a mutation Extreme cases are occasionally seen such as an infant so scaly at birth that it was nonviable reported by Shields and Bowman (APed 57 756 1940)

**Symptomatic Ichthyosiform Change (Xerosis)** is seen in pellagra, avitaminosis A, dehydration chronic debilitating disease and the like (Jeghers: NEngJM 228: 714 1943) A patient with lymphosarcoma and hepatic insufficiency exhibited acquired ichthyosis (Glazebrook and Tomaszewski: ADS 55 28, 1947)

**Ichthyosis Follicularis** is the name applicable to congenital ectodermal defect with follicular spines.





Figs. 755 and 756—Ichthyosis. (Dr George Lingenfelter)



Fig. 757—Ichthyosis hystrix.



Fig. 758.—Mal de Meleda.

**Mal de Meleda** is an hereditary ectodermal defect resembling keratosis palmaris et plantaris, with involvement of the dorsa of the hands and feet and spread onto the forearms, elbows, and legs, in association with dystrophy of the nails. Kogoj (ActaD-V 15: 264, 1934) described 9 cases from the Isle of Mljet, where it occurs, and suggested the name, *Keratoma extremitatum hereditaria progrediens.* The inheritance is as a recessive gene, and the frequency of its incidence is due to inbreeding.

**Keratoma Plantare Sulcatum** is a chronic affection of the soles, seen in natives of tropical countries who seldom wear shoes and whose feet are constantly subjected



Fig. 759.



Fig. 760.

Fig. 759.—Keratosis palmaris, hereditary. (Drs. Miller and Tausig.)
Fig. 760.—Keratosis palmaris hereditary: histologic structure.





Figs. 761 and 762.—Keratosis punctata, disseminated volar hyperkeratoses in a man whose [illegible] were unaffected [illegible] t age 14 years.

to irritation. The cause is unknown. The disease is characterized by marked plantar keratosis and by cracks which extend through to the corium and often become infected. Many of the keratotic masses become detached leaving characteristic, punched-out holes. Rest, combined with the use of a keratolytic, such as salicylic acid constitutes the best method of treatment. (Aars: ADS 24: 570, 1931.)



Fig. 763.



Fig. 764.

Fig. 763.—Keratoma plantare sulcatum. (Aars: ADS 24: 570, 1931.)
Fig. 764.—Porokeratosis. (Dr. Carroll Wright.)

Papillomatoses.—Rare and curious verruciform conditions classed under this title were reviewed by Wise et al. (ADS 36: 475, 1937; 39: 696, 900, 1939; 40: 432, 742, 1939). Gougerot and Carteaud (AfDuS 165: 232, 1932) described 3 new forms of papillomatosis, which are to be distinguished from epidermodysplasia verruciformis, verruca plana juvenilis, and Darier's disease: (1) punctate, pigmented verrucous papillomatosis, comprising two types, the punctate form of Gougerot and Clara and the verrucous form of Gougerot, Clara, and Bonnin; (2) confluent and reticular papillomatosis; and (3) nummular and confluent papillomatosis.

Epidermodysplasia Verruciformis of Lewandowski and Lutz (AfDuS 141: 193, 1922) exhibits lesions present at birth, with no site of predilection for the first lesions. The smallest are papules 2 mm. in diameter, round, oval, or polygonal, with perpendicular margins, smooth surfaces, and pale red or reddish violet color without pigmentation. There are scales which are grayish in places, thick, yellowish, greasy and removable in other areas. Lesions become disseminated fairly symmetrically over the whole body including palms and soles. Dorsa of hands and feet are usually affected. Plaques 1 to 2 cm. in diameter are the largest lesions, and transitional, confluent and lichenoid patches occur. The scalp is involved from childhood on. The lesions respond to x-ray treatment, but soon recur. Squamous carcinoma may eventually develop in some of them. Degeneration and vacuolation of the epidermal cells are found to extend as deeply as the basal layer. Their similarity to verruca planae is considerable, though disarrangement of rete cells and pyknosis and fragmentation of nuclei may distinguish them (Sullivan and Ellis: ADS 40: 422, 1939). Lutz (Dermatologica 92: 30, 1946) accomplished successful experimental inoculation of the disease from a woman to her sister.

Acrokeratosis Verruciformis (Hopf: AfDuS 167: 344, 1933) resembles epidermodysplasia verruciformis, affecting dorsa of hands and feet. It is less extensive in distribution, and the basket weave vacuolation, parakeratosis and degenerative epithelial changes of the latter are absent. See Loveman and Graham (ADS 43: 971, 1941) who judged their cases, a girl and her mother, to be nevoid.

Confluent and Reticulated Papillomatosis.—The onset has been between the fifteenth and twenty-fifth years, beginning in the intermammary region and there most

intense. Small warty papules 1 to ? mm. in diameter were present dirty gray in color lacking scaliness. The lesions tended to show median location on the trunk. Confluence occurred with the formation of reticulated patches isolated lesions being scattered about. The scalp was unaffected. The volar surfaces were not porokeratotic. Papillary ridges were found in the axillae. The eruption did not itch. The epidermis was slightly atrophic and the elastic tissue was severely damaged. In the case of Wise and Sachs (ADS 36: 4 5 1937) the absence of scaling was a difference from pityriasis versicolor. The intermammary and epigastric regions were involved particularly with confluence in the cente The mucosae were unaffected, and no systemic symptoms appeared. Histologic changes comprised mainly lamellated hyperkeratosis.

Nummular and Confluent Papillomatosis.—The one case began at 13 years of age in the intermammary region, spreading from there and most intense in the epigastric reg on. Small, verrucous papules, pale red spots, and pale red reticulum were the types of lesions present. No scales were present. Almost the entire trunk became involved with confluence of the nummular lesions. The scalp was unaffected, and the volar surfaces were not porokeratotic. Itching was severe. Histologic changes were in the elastica, not the epidermis.

Punctate Papillomatosis (Gougerot and Clara).—The one case began at 13 years of age, on lateral portions of the body spreading over trunk and head within a year, disappeari g in the autumn and winter. Punctate verrucous papules on the neck, trunk and extremities scaling stippled erythema of the scalp and face; and porokeratosis of the palms and soles comprised the three types of lesions found. On the face and scalp there were crusts, beneath which were small ulcers. The regions involved were the seborrheic ones. Treatment of all kinds failed.

Verrucous Papillomatosis (Gougerot Clara and Bonnin).—The one case began in adult life on the dorsum of the hands, wrists, and forearms. Later the palms, neck, and face were involved. The papules were elevated and rounded red to brown in color 1 or mm. high, 3 to 5 mm. across. The scalp and volar surfaces were not involved. It hing did not occur Treatment was without benefit.

## POROKERATOSIS

**Symptoms.**—The disease generally begins as a small, slightly elevated, wartlike papule which slowly enlarges peripherally and undergoes atrophy centrally so as ulti mately to give rise to a circinate or crescentic plaque with a smooth, atrophic or callused center and a sharply defined slightly elevated, seamlike border Coalescence may produce pol cyclic patches. The encircling dykelike border is grayish or brownish in color 1.0 mm. o more in height and commonly crowned with a linear horny ridge, which is a characteristic feature, and a slender furrow may run along its crest. Little milliumlik corneous bodies are embedded in the floor and in the sides and margins of the surrounding wall in some lesions. These masses, brownish or blackish in color and rounded or oval in shape are capable of being picked out. The mucous membrane l occasionally attacked the le as here being white opalescent and circinate or oval in outline Symptoms are slight The development an l spread of a lesion are tediously sl w

The cause is unknown. Most patients have been males. No age is exempt. Hered ty may be concerned (Gilchrist JCutDis 15 356, 1897); see Ducrey and Respighi (AnndeD 9 1 1898) Wende (JCutD 1 303 1898) succeeded in producing lesion by autotra plant tion. In con ideration of the usual fam lial history the absence of histologic ev dence of inflammat on, the spontaneou l sappearance f some cases, and the resistance f others to all but radical treatment Lain (UCutRev 22 383, 1923) interpreted the disease as a ariety f the peculiar and specialized nev Hall (ADS 18 341 1928) reporting Chinese cases, he thought them nevoid and approved Mibelli s original name, kerat atrophia nevus.

**Pathology.**—The hanges are mainly epid rmal, showing primaril an acanthosis with marked h perkeratos particularly about the gla dular orifices. Result ng pressure atrophy affect the rete the pap llary layer f the dermis, and the subjacent glands. Laminated corneum fill the mouth f the sweat duct and ult mately occludes their lumina. Both ha f llicles and glands are imilarly ffected by the gradual expansion of the plaque See Meischer (ArDuS 141 332, 1910) who preferred parakeratosis annularis as the name for this ep thelial d sease.

**Prognosis.**—The disease ma start in infancy (Rosen: ADS 43 782, 1941) and persist for life involut spontaneously See Jones and Smith (ADS 56 4.3, 1947)

**Treatment.**—Ex o may be desirabl ; t will cure

## CONGENITAL ECTODERMAL DEFECT

Anomalous formations of the ectoderm including its accessory structures are of occasional occurrence They are frequently associated with other physical characteristics so that the cases fall into distinctive groups Those showing (1) symmetric volar keratosis, with follicular keratosis of body or (2) keratoses of hands, feet, and body with leucoplakia of the mouth, or (3) these changes combined with corneal alteration or cataract.

Patients generally also present several of the following stigmas

Congenital dearth or absence of the sweat glands
Partial absence or hypoplasia of the pilosebaceous apparatus
Marked dental dysplasia
Thin glossy smooth, dry skin
Intolerance of heat
Alterations of nails, either hypoplasia or pachyonychia



Fig. 163.—Hypotrichotic congenital ectodermal defect, sister and brother (Dr O. G. Costa )

The facial appearance is usually peculiar The prominent frontal bulge is due to exostoses of the inner table of the skull as is also the depression of the base of the nose which is relative and not due to destruction of the nasal bones as in syphilis (Thannhauser J 106 908, 1936) Fine wrinkles are seen about the eyelids and oral commissures. There is an hereditary tendency and while this appears dominant and transmitted through mother to son, in other families it is not sex linked and may affect females.

Weech (AmJDisChild 37 66, 1929) clearly distinguished the anhidrotic group whose difficulty in perspiration makes them intolerant of heat. He thought the cone-shaped incisor especially significant Milia are frequently present, especially about the knees and elbows, in patients having normal nails and teeth but lacking hair (Sweitzer ADS 27: 1017 1933) These hair and nail dystrophies occur in either sex and are transmitted by either sex, whereas the inheritance of the anhidrotic hypotrichotic-anodontic group is like that of hemophilia, cases in the female being exceptional (de Silva: QJM 8 97 1939 review of 48 cases and bibliography) The classic triad in these cases consists of anhidrosis, hypotrichosis and dentia or severe abnormality of the denture. Fever and headache affected 3 brothers with this abnormality when they got hot, and no eccrine glands were found in biopsies of their skins by Sanderman (AIntM

67: 846 1941) Sweat glands are scarce but not absent in other cases which may be called hypohidrotic (Felsher ADS 49 410 1944)

Rothmund s Syndrome.—Appearing in the first weeks of life and occurring collaterally in sisters and brothers, this abnormality is recessi e in contrast with the usual dominant character of anhidrotic ectodermal defect and it involves more than the

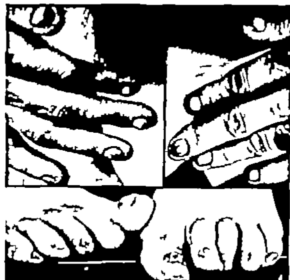


Fig 766.



Fig. 767

Fig. 766 —Pa hyonychia congenita. (Dr D. E. H. Cleveland.)
Fig. 767 —Congenital ectodermal defect, with alopecia. (Dr V Vermooten.)



F x 768 —Epidermodysplasia verruciformis. (Dr O G. Costa)

epiderml alon Cataract and poikiloderma w th tela gectasi are the distinguishing features (Thannhauser AnnIntM 3 559 1943; J 130: 38 1946) The sisters reported by Cole et al. (J 1?? 723 1945) exhibited almost total alopecia, atrophy of nasal mucosa hyp plasia f the nail anhidrotic dysplasia of the skin, which was mottled with dull red confluent l ghtly depressed nd mildly indurated zones, congenital cataracts with extreme internal strabismus and leucoplakia oris. Halley et al. (ADS

44 845 1941) described a girl with telangiectases, pigmentation defective teeth, and cysts in the iliac bones. Vitamin A was disappointing in the patient of Wise (ADS 48: 660 1943) but it provided much improvement for the patient of Anderson (ADS 51: 234 1945), a woman whose glucose tolerance curve was diabetic. Androgenic medication helped the brothers reported by Garb and Rubin (ADS 50: 191 1944)

**Werner's Syndrome** includes progeria-like thin, atrophic, stretched skin which undergoes spontaneous ulceration on the exposed parts. The sclero poikilodermatous abnormalities do not appear until the second or third decades of life and the skin changes are not those of true scleroderma.

**Etiology**—Little is known about the cause of these disturbances. Since some cases appear as mutants, one is led to take note with interest of the fact that particular forms of mutation result in exceedingly similar abnormalities there is a family resemblance between unrelated patients

**Treatment.**—As in ichthyosis, the patient must learn to live with his skin. If he cannot sweat, he must avoid heat and exertion. Judicious paring or sandpapering of lesions may be worth while. Fissures and infections must be treated appropriately Plastic repair of the nasal deformity was described by Lewin (AOtol 35 210 1942)

## PACHYONYCHIA CONGENITA

The nails are thickened opaque, lusterless, and folded longitudinally Follicular keratoses somewhat like ichthyosis hystrix are found in the flexures often they are thick, scaly and blackish or greenish in color Volar keratoses in disseminated patches are found the patches frequently encircling the fingers so as to affect the dorsal as well as the volar surfaces Leucoplakia and anomalies of the hair sometimes coexist (Drasio: ADS 30 _18, 1934)

## EPIDERMOLYSIS BULLOSA

Epidermolysis bullosa is a peculiar condition of the skin, usually hereditary characterized by the development of vesicles and bullae on even slight traumatic provocation. The disease is divisible clinically into two main groups, the simple and the dystrophic, and the latter can be subdivided into three classes inherited in different ways (Hundley and Smith SMJ 34 364, 1941) The cause is not known. Symptoms are usually worse in warm weather The severity of the disease ranges from extreme fragility such that the newborn soon dies (Black et al. J 129 734, 1945 Lamb and Halpert ADS 56 369 1947) to trivial involvement Mild cases are nevertheless likely to unfit one for military service (Leider and Baer ADS 46 419 1942) Mucosal involvement is rare, but it may interfere with a baby's nursing (Corson ADS 49 382, 1944)

Strands of fibrillar tissue normally extend from the dermis, terminate among the basal layers *of the epidermis, and probably have a function in* binding down the epithelium to the dermis. Such fibers are absent both from the lesions and from the uninjured skin of some cases of epidermolysis (Engman and Mook JCutDis 28 276 1910) It is difficult to understand how the disorder could be influenced by treatment. Atrophy and scarring are the sequelae of trauma, which is carefully to be avoided (Tulipan ADS 37 22, 1938)

**Localized Epidermolysis Bullosa** is recognized, the feet alone, or feet and hands, being the only sites where noninflammatory bullae appear especially in warm weather following minimal trauma, healing without scar sometimes associated with hyperhidrosis, and manifesting inheritance as dominant without accompanying dystrophies (Elliot: JCutDis 13 10, 1895 Mouney ADS 50 16 1944; Johnson and Test: ib. 53 610,



Figs. 769 and 770.—Epidermolysis bullosa, hereditary (Dr Grover Wende.)



Fig 771.—Epidermolysis bullosa. (Dr T W Allworth )



Fig 772.



Fig 773.

Fig. 772.—Epidermolysis bullosa linear bullae. (Dr Norman Tobias.)

Fig. 773.—Epidermolysis bullosa histologic structure Note loss of elastic fiber in the superficial part of the dermis. (Dr Stuart W y )

1946) The case of Kierland and Harrison (PSMMC 15 318, 1940) showed marked elevation of urinary porphyrins, and the elastic tissue seemed not abnormal. The disease received attention during the war because military life proved intolerable to persons whose fragile skins tolerated less strenuous enterprise (Greenberg ADS 49 333, 1944, Franks et al.: UCutRev 40 57 1945; Waisman: J 1.4 1247, 1944) An elastic bandage from ankle to knee seemed to reduce vulnerability of the feet reported Wiser and Orman (ADS 5.: 317 1945) Cockayne (BJD 59 109 1947) thought the condition a separate entity rather than a variant of epidermolysis bullosa. It is also to be distinguished from tinea, pompholyx and impetigo, though these may complicate it secondarily

## CONGENITAL SKIN DEFECTS OF THE NEWBORN

Circumscribed absence of the skin is in rare instances observed in the newborn. The defect is often solitary but lesions may be multiple and are then usually grouped or symmetric The outline is sharply defined and circular or oval in most instances. The diameter is rarely more than 3 cm. The subcutaneous tissue is little affected, and there is no evidence of inflammation. The site of predilection is the vertex of the scalp, but Helm's case presented integumentary loss over a large part of both sides of the trunk and in Abt's the defect involved the anterior aspects of both knees (AmJDisChild 14 118 191 ) Microscopically one finds absence of epidermal structures, but no evidence of degeneration. The cause is unknown, though amniotic adhesions have been blamed. The lesions bear no relationship with trauma during parturition. They generally granulate and heal, but without the development of epidermal accessory structures (Sutton ADS 31 863 1935 Anderson and Novy ib. 46: 257 1942) Congenital skin defect may be a manifestation of epidermolysis bullosa (Prakken Nederl. Tijdschr geneesk. 83: 2440 1939)

## NEVUS

Nevus is a generic name for a malformation usually localized and usually congenital. Nevoid signifies abnormality of development. One notes that growth and development do not end with the event of birth. The name is loosely used, being applicable to pigmented moles especially and also to *hemangiomas*, *linear defects* characterized by hyperkeratotic and verrucose anomaly and other malformational abnormalities.

**Pigmentary Nevi** are circumscribed tumors or superficial infiltrations composed of specific nevus cells. The macular or papular pigmented lesions are usually present at birth. In color they range from pale fawn to bluish black, and in size from a millimeter to many centimeters in diameter In rare instances large areas may be involved. Large growths are identical with small ones, although certain features may be exaggerated. The lesions may be solitary or many In outline they are usually rounded or oval, but in shape, hairiness and distribution, they are subject to great variability They are usually congenital, but their development may be delayed even until puberty Accessory mammary structures resembling pigmentary nevi are of frequent occurrence and should not be mistaken for them Extensive nevi of both vascular and pigmentary types are sometimes associated with similar alteration of the leptomeninges (Netherton ADS 33 238, 1936 Wilcox AmJDisChild 57 391 1939)

There may occur nevoid hyperplasia of almost any cutaneous structure The changes may be confined to the sebaceous glands and periglandular structures, to the follicles, or to the epidermal stratum Malformation may be primarily *mesodermal rather than ectodermal*

**Nevus Cells** are usually large pale, and angular in outline with oval, vesicular nuclei. They may be tightly packed small, and hyperchromatic; they may undergo atrophy and come to resemble fibrous tissue as in soft fleshy moles. They may be massed or arranged in columnated groups. Pigmentation, variable in quantity is due to the

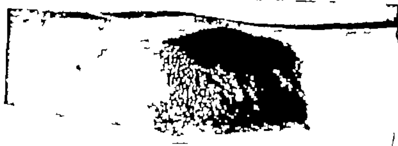


Fig. 774 — Pigmentary hairy nevus, elbow



Fig. 775



Fig. 776



Fig. 777

Fig. 775 — Pigmentary hairy nevi "bathing trunk" lesion and disseminated moles. (Dr F Ronchese.)

Fig. 776 — Pigmentary nevus benign melanoma.

Fig. 777 — Benign melanoma, showing nevus cells.

presence of intracellular iron-free amorphous brown granules of melanin. Pigment bearing cells have been thought epidermal in origin, or dermal, or both, but this is controversial. Masson supported the theory of origin of nevus cells in nerve tissues and described the structure of the nevus as resembling Meissner corpuscles and neural tubes, the nevus cells in the upper dermis being arranged on these tubes like flowers on a stem. Nevus cells are dopa positive. Ebert (ADS 37: 1 1938) called attention to the clear cells of Merkel occurring in the basal layer of the epidermis, and these he believed not to be tactile cells in fact, but to be the parents of nevus cells when anomalous. Proliferation of these cells would produce the histologic picture of intraepithelial formation of nests. Interpreting spatial proximity as indicative of derivation, Montgomery and Kernohan (JInvD 3 465 1940) argued that dendritic cells are simply altered basal cells, that cellules claires are modified dendritic cells, and that multiplication of clear cells leads to the formation of nests of nevus cells in the epidermis. Such nests appear to drop down into the dermis from their epidermal site of origin, and these authors claimed to have demonstrated the epidermal origin of nevus cells in the majority of cases studied. Traub and Kiel (ADS 41 314, 1940) classified nevi histologically as intraepidermal, intradermal, junction (those at the dermo-epidermal border) combination types, and blue nevi. The junction nevus they judged most hazardous. Becker (Trans ADA 1947) called lesions with nevus cells only in the epidermis type a, those superficially located in the dermis type b, and those deep in the dermis, associated with structures of Meissner's corpuscle and neural sort, type c. Combinations such as a plus b, b plus c, and a plus b plus c are common. When histologic indications of nevus cell invasion of the epidermis are present, the lesion is especially hazardous, Becker noted. Silver impregnation stains were studied by Jaeger (abs YBD 1946 p. 512) who found in intimate connection with nevus cells numerous neurofibrils from the myelinated trunks of the hypoderm.

**Prognosis.**—Pigmentary nevi sometimes become malignant. A hairy pigmented nevus only rarely does so. *Increase in size*, *increase in pigmentation* and *irritability*—these three symptoms singly or together are the early clinical evidences of change from benign to malignant melanoma.

**Treatment.**—Destruction should be complete and should unhesitatingly include normal tissue beyond the periphery and depth of nevus tissue if there is doubt about the lesion's being benign. This destruction should be accomplished in one treatment, not piecemeal. Excision is satisfactory (Phillips TexasSJM 42 645 1947). Most quiescent nevi should be let alone.

**Mongolian Spots.**—See p. 549.

**Halo Nevus.**—The lesion is rounded, the area [illegible], and in its center is a small brownish maculopapule, nest of melanophores in the dermis. Sutton's disease; see Feldman and Lashinsky (ADS 34 800 1936); Kaske (abs ADS 55 266, 1947); Leider and Cohen (ADS 5 390 1949).

**Blue Nevus** is a blue black, oval, slightly elevated firm lesion usually located on the face or the dorsum of a hand or foot. The epidermis and upper cutis are normal, but in the dermis are circumscribed regions containing long irregular spindle cells filled with melanin. These are benign almost invariably (Montgomery and Kahler AmJCa 36 527 1939).

**Anemic Nevus.**—See p. 394.

**Atrophic Nevus** resembles linear atrophic morphea (Andrews ADS 50 283, 1944). Compare hemiatrophy p. 561 and hemangioma p. 393.

**Cerebelliform Nevus** is a large corrugated lesion which may cover half the scalp, composed of specific cells and neurofibromatous tissue (Klaber BJD 57: 16, 1945). See Fig 782 on p. 579.

**Amelanotic Nevi.**—These growths are similar to pigmentary nevi, but lack pigment. *When small* may be large, corrugated, and cerebelliform. The nonpigmentary type may be called *amelanotic melanoma*. Rarely is one malignant, but they may become so. *Schwannoma* is the title Becker (ADS 30 779 1934) applied to them, interpreting them as representative of proliferation of deeper nerve structures. See Neurilemmoma, p. 549.

**Naevus Lipomatosus Subepidermalis** is a rare anomaly in which groups of [illegible] intracutaneous fatty tumors [illegible] simulate [illegible] circles in the skin (Ormsby [illegible]

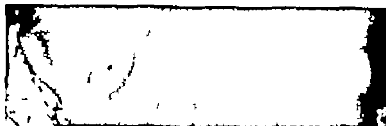


Fig. 778.—Leucoderma acquisitum centrifugum; "halo nevus"



Fig. 779



Fig. 780

Fig. 779.—Naevus sebaceus

Fig. 780.—Naevus sebaceus, showing composition of huge fat glands.



Fig. 781.—Linear verrucous nevus; naevus unius lateris (Dr J. P. Quequierra)



Fig. 782.



Fig. 783.

Fig. 782.—Anemic nevus, nuchal.

Fig. 783.—Cerebriform nevus, huge, of occiput (Hammond and Ransom A.Surg 35 309 1937)



Fig. 784.—Comedo nevus (nevus follicularis keratosus). A girl whose sibs are unaffected. Onset as brownish discoloration at 6 weeks of age. Acneform lesions present during past few years. 1 Bands of comedo-like lesions. 2, Tissue excised from axilla by Dr Curtis Abbott to prevent recurrence of disabling inflammatory nodules as of hidradenitis axillaris. 3 Gross section of excised tissue showing cysts and comedones. 4 Palmar pits which constitute the acral termination of band extending down the forearm. 5 Side of chest, showing scars from acneform lesions. 6 Distribution along line alba, and acneform lesions on the abdomen. (Patient of Dr R. O. Hughes.)

**Naevus Sebaceus.**—The lesion is an unctuous, yellowish one with a soft granular surface pitted by the hypertrophic orifices of the overgrown sebaceous glands, the yellowish bodies of which elevate the epidermis slightly (Savatard: BJD 53: 14, 1941). The patches may be isolated or may occur in systematized groups as a linear nevus. They appear soon after birth and rarely exceed 5 cm. in diameter. The scalp is a common location; the lesion here is partially bald. Carcinoma may develop in them, rarely. In some sebaceous nevi the epithelium is excessive and keratinization is seborrheal; they resemble acanthotic nevi, from which they are distinguished by yellowish, pitted papular elements at their periphery.

Sebaceous nevi are to be distinguished from adenoma sebaceum and from *hypertrophic sebaceous glands* which are isolated, umbilicated, yellow papules (Gillman: ADS 35: 633, 1937). The latter sometimes follow the squeezing of comedones in seborrheal milk-drinkers.

**Naevus Syringocystadenomatosus Papilliferus.**—These rare lesions are papules of millet seed to hemp seed size usually arranged in groups. They are pinkish but translucent and vesicular inclusions may be detected. Some papules are umbilicated, simulating molluscum contagiosum. Isolated lesions occur but often they are confluent, and the plaques may be of considerable area, or systematized. Microscopically one finds the sweat ducts, cystic and papilliferous, emptying onto the surface through a thickened epidermis (Sachs and Lewis: ADS 36: 1?0?, 193?). The corium is permeated with nevus cells. Digitations push into the dilated sweat ducts, and support an inner columnar and outer cuboidal layer of sweat-duct epithelium, which rests on delicate connective tissue. Excision is simple and satisfactory treatment.

**Naevus Follicularis Keratosus (Comedo Nevus).**—This systematized malformation, usually unilateral, is manifest as fillets of comedonelike lesions. Dilated follicles are filled with epidermal detritus, and some of them are cystic. The crateriform or sievelike depressions dip into the skin along the direction taken by the lanugo hairs in the same region. The comedo-like lesions and cysts commonly undergo acneform inflammation, with the formation of tender nodules which may resorb, or discharge and heal with atrophic scarring. Portions of the anomaly may require excision (Sutton and Sutton: Dis of Skin, Mosby 1939).

**Dermatosis Papulosa Nigra.**—Minute hyperpigmented, hemispherical papules develop in small numbers symmetrically on the malar regions or below the eyes as a common affection of Negroes. These benign lesions show microscopically *irregular acanthosis, excess of pigment in the basal layers of the epidermis, and anomalous* pilosebaceous structures (Michael and Seale: ADS ?0: 620, 1939).

**Connective Tissue Nevi** are unusual but Steiner (ADS 50: 1?3, 1944) collected several, the name for which may be given as *Naevus Elasticus*. The papules or lichenoid nodules of tiny size and whitish or brownish color, discrete but closely set together and simulating tiny cobblestones, are often systematized in bands, asymptomatic and present since earliest childhood. Collagenous or elastic tissue alterations or both may be found.

**Linear Nevus (Naevus Unius Lateris)** is a nevoid growth which is arranged in fillets or streaks (see Ichthyosis hystrix). Such may be unilateral or bilateral, involving one or several zones. They may be of various structures, including those which are pigmentary, papillary, verrucose, sebaceous, or comedo-like (Melczewski: BJD 54: 90, 129, 194?). Ichthyosiform nevi involving mucous membranes are known. If the nevus reaches the midline of the abdomen, its distribution there follows the linea alba.

In linear nevus many theories have been suggested to explain the peculiar arrangement. Montgomery (JCutDis 19: 4?3, 1901) reviewed these theories: that the lines follow the course of the cutaneous nerves; the lines run along Voigt's lines, the boundaries of peripheral nerve distribution; the lines follow the lines of cleavage of the skin; the lines follow the course of the blood vessels; the lines run in the metameres or segments of the body; the lines follow embryonic tissue expansions, the trends of growth of the tissues. The disorder is plainly one of organization, and research in experimental embryology may throw light upon the mechanisms involved (Huxley and DeBeer: Experimental Embryology, Cambridge U Press 1934).

## MELANOMA

**Symptoms.**—Malignant, pigment bearing nevus-cell tumors usually but not invariably start in a pigmentary nevus. A small primary lesion may be overlooked, and sometimes careful search reveals none at all. In the series of 317 cases of Affleck (AmJCa 27: 120, 1936) 268 developed



Fig. 785.



Fig. 786.

Fig. 785.—Malignant melanoma, toe. (Drs. Butterworth and Klauder.)
Fig. 786.—Melanotic whitlow, thumbnail bed.



Fig. 787.—Malignant melanoma, cancerous nodule developing in melanotic nevus of buttock. (Drs. Butterworth and Klauder.)



Fig. 788.



Fig. 789.

Fig. 788.—Malignant melanoma, widespread metastases. (Dr. Parkins.)
Fig. 789.—Malignant melanoma, widespread metastases. (Dr. Schalek.)

from pre-existing nevi, none of which was hairy While almost all nevi remain benign throughout life, it is impossible to predict in a given instance whether this will be the case Therefore all such lesions are potentially dangerous. Those on the head and feet and those which are especially liable to irritation are the most likely sources of trouble (Butterworth and Klauder J 102 739 1934) Increase in size and increase in depth of pigmentation are definite danger signals, as are also increase in vascularity and an apparent chronic infection with slight tenderness (Brown and Byars SGO 71 409 1940) In melanotic whitlow the process first becomes apparent around the border of the nail (Hertzler: ADS 6 701 1922 Pack and Adair Surg 5 47 1939) and is to be distinguished from paronychia felon granuloma pyogenicum subungual hematoma, chancre, and gangrene

Ulceration and bleeding are late symptoms. They mean that action has been delayed until it is probably too late. The primary tumor enlarges, becomes nodular papillomatous, perhaps fungating and sloughing, and intracutaneous satellites appear about it. The disseminated cutaneous lesions are pinhead to egg size ovoid, moderately firm in consistency and brownish or blackish in color

The course of the disease generally is rapid. Metastasis first reaches regional lymph nodes and is there limited for a time but becomes general via the blood stream. The liver and lungs are commonly invaded in a massive manner and the heart brain and other organs become widely infected. The patient generally maintains a fair state of well-being until the terminal stage, then declines rapidly The coloring matter is melanin, not blood pigment as in Kaposi s tumor Pigment is present in the secondary growths, and may be present in the urine General pigmentation may occur especially of the exposed parts (Odel et al PSMMC 12 742, 1937)

**Amelanotic Melanomas** are recognized (Farrell ADS 26 110 1932) They differ only in lacking the pigment which is more or less profuse in ordinary melanoma

**Pathology**—In view of doubt regarding histogenesis of the lesions, the name melanoma has met with approval (Dawson EdinMJ 32 509 1925) See nevus cells (p 575) and pigment formation (p 7) Melanoma is the neoplastic proliferation benign or malignant of melanoblasts, which are normally found in pigmented epidermis. Melanoma cells are dendritic in vitro and their processes are full of granules they do not resemble ectodermal cells (Grand et al. AmJCa 24 36 1935) Pathologic changes indicative of malignancy are hard to describe Invasion of the epidermis is suggestive of malignancy of a nevus (q v) the junction type of which is the most hazardous. Becker tells us that melanin granules which tend to be of the same size within one cell in benign or malignant lesions, are more varied in size and quantity in malignant moles than in benign ones. The neurogenic origin of the cells is argued as acceptable in the interesting symposium of Moir Dawson et al (BJRadiol 19 217 1946) See also Innes et al (EdinMJ 46 695, 1939) Dependence is to be placed on the history of progress in the lesion.

Melanoma develops from pre-existing presumably once benign nevi in many instances, or it may commence de novo in the skin, eye or elsewhere Melanoma has been observed to be present at birth (Sweet and Connerty: AmJDisChild 62: 1029 1941) Transplacental infection is recorded (Weber et al: BMJ 1: 537 1930) A case simulating Paget s disease was described by Stout (AmJCa 33: 196, 1930) Melanoma appeared in lymph nodes without a discernible primary in a patient whose arsenical dermatitis has healed with generalized spotty pigmentation (Rothman and Felsher:



Fig. 790.



Fig. 791.

Fig. 790.—Malignant nodule developing in a malignant lentigo or junction melanoma.

Fig. 791.—Malignant melanoma and the nodes into which it has already metastasized.



Fig. 792.—Malignant melanoma, composed of melanin-laden spindle cells.



Fig. 793.—Malignant melanoma showing nests of malignant cells, intraepidermal on the left, intradermal and accompanied by inflammation on the right. (Dr. Stuart Way.)

ADS 52 64 1945) Extensive hairy pigmented nevi are only rarely the site of its origin (Ebert and Oliver ADS 46: 604, 1942; Conway Surg 6: 585 1939) Numerous instances have been reported occurring in Negroes (Anderson Surg. 9: 425, 1941; Imler and Underwood: SouthSurg 13: 61 1947) Rarely does a child die of melanoma, reported Spitz (AmJPath 24: 591 1948); the abrupt rise in malignancy after puberty suggests a hormonal influence in the acceleration of growth.

**Diagnosis** requires differentiation from seborrheic keratosis, hemosiderinotic histiocytoma blue nevus, pigmented basal cell tumors, and small purplish angiomas (Montgomery MCNAm 28 968, 1944) Microscopic examination provides the final criterion.

**Treatment.**—Melanoma which seems not to have disseminated should be excised radically (Taussig and Tonney CalWM 52 15 1940; Driver and MacVicar J 121 413 1943) The electric needle or other half measure will prove disastrous. Klauder (J 102 739 1934) used electrosurgery excising a 3 cm. margin of apparently normal tissue, including the deep fascia, an important measure. Complete excision of a mole is harmless, entails no danger and gives protection against possible malignant change Bloodgood expressed the idea of prevention in the slogan major diagnosis and minor surgery Melanoma is not to be attacked by x ray for the lesions are only exceptionally radiosensitive (Ellis BJRadiol 12 327 1939)

After removal of the primary lesion Pack and Wuester (SouthSurg 9 775 1940) demonstrated that foci could be found in the regional nodes in as many as half the cases Some cases with regional node metastases have been cured (Daland and Holmes NEngJM 220: 651 1939) and the increased probability of cure by adequate surgical work should not be denied any patient Howes and Birnkrant (AmJSurg 60 182, 1943) recommended the routine dissection of the lymphatics, and Turner (BMJ 1 81, 1939) and Pack et al (CalifM 66 283 1947 SMJ 40 832, 1947) have left no doubt that greater saving of life will result from the en masse excision of the primary lesion with its entire lymphatic drainage basin and the dissection of the regional nodes in continuity See Gordon et al (The Biology of Melanoma, NYAcadSc, 1948)

## NEUROFIBROMATOSIS

**Symptoms.**—The lesion of the Smith Recklinghausen disease (Fulton NEngJM 200 1315 1929) develop in and beneath the skin as sessile pedunculated or flattened, painless tumors. They may be present at birth, but usually appear at or after the age of puberty The onset is said in many cases to have followed unusual exposure to cold. Multiple skin tumors are often associated with nerve tumors. Anomalous pigmentation, particularly in the form of coffee spots, and imbecility and epilepsy are occasional accompaniments. Osseous and endocrine changes are sometimes noted. Heredity is involved in only about 15 per cent of the cases. Occasionally the growths may be single, pendulous, and large. As a rule they are multiple, numbering from 3 or 4 to 100 or more. In size they range from that of a small pea to that of a turkey egg They are usually velvety smooth, rounded or oval, with a narrow and somewhat elongated neck, but they may be pear or sausage shaped, or even lobulated and sessile or even subcutaneous. In their early stage, and in some instances throughout their course, elevation is slight or wanting and the tumors are more apparent to touch than to vision The integument covering the tumors is pinkish in



Figs. 794 and 795.—Smith Recklinghausen disease, showing myriads of nonpigmented, elvsty protuberances, and their appearance at close range. (M Emil Formay)



Fig. 796.—Elephantiasis scrotorum. (Richards b ADS 3 182, 1921.)

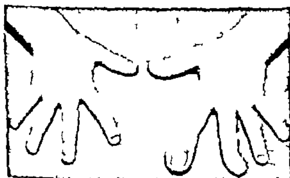


Fig 797



Fig 798.

Fig. 797.—"Local" overgrowth of left thumb, index finger and middle finger (Chandler J 109 2411, 1937)

Fig. 798.—Cutis verticis gyrata (Drs. Kessler and Kessler)

color lax, and soft. The trunk is a favored site for the lesions, but the face and limbs are frequently affected The mouth the rectum, in fact the entire intestinal tract and even the bones may be involved. Formes frustes occur and the lesions may be unilaterally limited in distribution to the region supplied by a nerve, especially by branches of the trigeminal.

Cases fall into 4 groups: (1) plexiform neuroma, without multiple molluscoid tumors, and with or without pigmentation (including elephantiasis nervorum, macroglossia, and local overgrowth); ( ) multiple molluscoid tumors without obvious nerve trunk tumors, and with or without pigmentation; (3) pigmentation without (or as yet without) obvious nerve trunk or cutaneous neurofibroma; and (4) anomalous cases, complicated with lesions of the bones or epidermic changes, this group including the famous elephant man (Levin and Behrman ADS 41 480 1940; Wise and Eller: J 86: 86 1926)

GASTROINTESTINAL INVOLVEMENT.—Megacolon in a horse was shown by Pick (Beitr z. path. Anat. 71 560, 1922) to be due to neurofibromatosis of the splanchnic nerves which supplied that portion of the gut. See Neurilemma.

PIGMENTATION.—In some generalized cases freckling and pigmentation are fairly characteristic, but not pathognomonic, accompaniments. Pigmentation may precede or accompany tumor formation.

PREGNANCY.—There usually occurs growth of the tumors during pregnancy along with increase of pigmentation and the development of pain or tenderness in the nodules.

OSSEOUS INVOLVEMENT.—Bone cysts associated with pigmentation of the skin are described. Unsuspected bone lesions may be found by x ray examination of patients with cutaneous involvement. Cushing (Tumors of the Nervus Acousticus, Saunders, 1917) with a report of 13 cases, first stressed the association of acoustic nerve tumor with neurofibromatosis. Bone cysts, chloasma, and premature puberty (Robson and Todd Lancet 1: 377 1939) may belong here see osteodystrophia fibrosa, p. 390.

MALIGNANT COMPLICATION.—It is rare for malignancy to supervene; when it does, it is generally in the form of locally recurrent spindle cell sarcoma (compare dermatofibrosarcoma see Speed AnnSurg 116 81 194 ) Deep neurofibroma re dangerous (Caracho AmJSurg 41 275 1938) These lumps are movable, noninfiltrated tumors, scapular axillary gluteal abdominal, and of the extremities. Radical surgery is the best treatment.

OTHER FEATURES.—Adenoma sebaceum is said to be a frequent concomitant. While some a thors attempt to unite within one yndrome v Recklinghausen's disease and the combination of tuberose sclerosis with Pringle s disease (q v under Adenoma sebaceum) the two can be distinguished linically and histologically and coexistence of the two has not been demonstrated. Complications nclude deafness (16 per cent) pain (1_ per cent) hemorrhage (10 per cent) psychosis (3 per cent) and malignancy (1 per cent) S rgical complications were discussed by Jones and Hart (AnnSurg 110 916 1939) including the possibility of hemorrhage into a pachydermatocele.

The interrelationsh ps between epilepsy neurofibroma, and nevi grouping them all under the designation ectodermoses, were considered by Yakovlev and Guthrie (ANeurP 26 1145 1931) They called ttention to the common systemat ration, apparently neural, w th in ol ment of one or a group of cutaneous nerves, particularly the trigeminal.

Elephantiasis Nervorum ) the name applied when a limited region is invol ed in a d ffuse manner so that the part is grossly enlarged r deformed. Cases in which the scalp wa affected were collected by Helmholz and Cushing (AmJMSc 132: 335, 1906) Th commonest location the scalp, and the lesion is likely to begin as brown spot which early years begin t mg. An extremity is a possibl location for h a pa hy lermatocele The nvolveme t i likely t be unilateral. Compare Cuti ert cis gyrata. Dermatolysis nd cut hyperelastica are probably Recklinghausen disease w th widespread peripheral distribut on They too, are somet mes unilateral. The broad lax, pendulou tumors which sometimes occur Recklinghausen disease appea t onsist ma nly f flat ml thickened skin, and generally i volve the face arms, xillae buttocks or thigh Eichenlaub (ADS 3 15_ 19*1) reported a case which clinically resembled a linear nevus the tumor in olved the forearm and consisted f a pendulous, lobulated, doughy mass, present since birth (Fig 196)

LOCAL OVERGROWTH wa the t tl Chandler (J 109 1411 1937) gave t remarkable gigantesque deformities f one or se ral d gits, without other pathologic alteration. The part appears imply magnified Rogers (BJS 16 681 1929) proved by dissection that such lesion are d to neurofibrom tosis.



Fig. 799.



Fig. 800.

Fig. 799.—Von Recklinghausen disease. (Drs Anderson and Tice.)
Fig. 800.—Cutis hyperelastica. (Dr Everett Lain.)



Fig. 801.



Fig. 802.

Fig. 801.—Cutis hyperelastica, scars, pseudotumours, and ulcer. (Dr Paul Otto.)
Fig. 802.—Cutis pendula, form of neurofibromatosis.

**Dermatolysis** was the name given by Wise and Snyder (JCutDis. 32: 139 1914) to a disorder manifested by sessile, doughy lumps of disseminated distribution.

**Cutis Verticis Gyrata** is a harmless but unsightly abnormality of the scalp in which the skin is overabundant and thrown into waves and folds with roughly sagittal axes. This syndrome may be caused by chronic inflammation, acromegaly myxedema, mycosis fungoides and nevoid or neurofibromatous malformation, according to Fischer (AfDuS 141 351 1922) See Zeisler and Wieder (ADS 42: 1092, 1940) Plastic surgery may be practicable (McConnel and Davies: AnnSurg 118 134, 1943)



Fig. 403.—Molluscum fibrosum gravidarum.



Fig. 404.—Neurinoma of tongue.



Fig. 405.—Neurofibroma, histologic structure.

**Cutis Laxa.**—The amount of hypertrophy and degree of looseness are greatly variable, but the affected skin is usually thickened and more or less pigmented, and is so loosely fixed to underlying structures that it hangs in baggy folds. The lesions are otherwise asymptomatic The microscopic structure is that of neurofibroma.

**Cutis Hyperelastica.**—The skin is smooth, soft, and apparently somewhat thinned. It is extraordinarily supple and elastic, however and when a fold is drawn out from

the body and released it may return to its original position with an audible snap like that of a rubber band. Laxity is especially marked about large joints. It may be general or confined to certain regions. The *Ehlers-Danlos syndrome* comprises (1) pronounced fragility of the skin and its vessels so that even slight trauma produces hematomas and wounds that refuse to remain stitched; (2) the healing of these with the formation of pseudotumors; (3) hyperelasticity of the skin; (4) hyperflexibility of the joints; and (5) lineae distensae which, with scars and peculiar molluscoid lesions on the exposed parts, are conspicuous features. Loose, pea size spherules, firm to the touch but fatty under the microscope, are found in numbers, especially in the loose skin of the extremities, where they sometimes undergo calcification (Holt: AmJR 55: 420 1946) See Tobias (ADS 30 540, 1934) Barber et al. (BJD 53: 97 1941) Carney and Nomland (ADS 56: 794, 1947)

**Neurilemmoma (Neurinoma, Schwannoma, Peripheral Glioma).**—The lesions are benign and movable except for their attachment to the nerve sheath from which they arise. Some authors have believed that the lesions of v Recklinghausen's disease are not of connective tissue origin, but that the fibers are nerve fibers and the cells are sheath cells of Schwann (Becker: ADS 30: 799 1934) These tumors are composed of reticular tissue in bands, the cells resembling those of Schwann, in areas reproducing organoid structure suggestive of Meissner's tactile corpuscles. Small intradermal tumors closely resemble nevi; in fact the hemispherical, colorless, firm, smooth nevi are probably of this type. The tongue is a relatively common site and they occur along the gut and in the mediastinum. Simple excision is curative.

**Molluscum Fibrosum Gravidarum** is a peculiar variety of fibroma in which the lesions develop during the later months of pregnancy and partially or completely disappear postpartum. The tumors are pinhead to pea size, pedunculated, and almost exclusively confined to the nuchal and mammary regions.

**Cutaneous Tags of the Neck.**—Similar tiny fibrotic outgrowths are frequently observed about the neck, especially the anterolateral aspects, of women more often than men (Templeton: ADS 33: 495 1936) Perhaps these lesions are verrucae planae, disseminated by cold cream. They are not apparently influenced by endocrine relationships. They are easy to destroy individually with a pointed cautery

**Etiology.**—The cause of neurofibromatosis is unknown Its association with endocrine disturbances is probably as cause rather than effect

**Pathology.**—The histogenesis is still debatable. V Recklinghausen held that the lesions are neurofibromas, and that they spring primarily from the connective tissue sheaths of the nerves, afterward spreading upward along the nerves. Nerve fibers run through them, usually widely separated from each other The specific histology was described by McNairy and Montgomery (ADS 51 384, 1945) Melanotic nevi, occurring coincidentally are probably essentially distinct

**Treatment.**—If the malformation is limited to a small region, such as one side of the face the lesions may be excised or otherwise destroyed with a view to cosmetic improvement. In widespread cases nothing can be done and the lesions are best let alone for fear of their recurrence. Improvement followed the administration of sulfathiazole, 2 gm per day given for another purpose (Weiss J 128 909 1945), and Paul Hemphill showed us (1947) a woman whose lesions diminished notably under treatment with fibrolysin by injection.

## TELANGIECTASIS

Telangiectases are dilations of small blood vessels. They are usually localized, but may be widespread in distribution. They presumably result from the enlargement of pre-existing vascular channels. Telangiectases are symptomatic manifestations of rosacea angiokeratoma morphea, roentgen dermatitis and xeroderma pigmentosum and they result from the distortion provoked by any expanding intracutaneous tumor The lesions are manifested as abbreviated and tortuous bright red lines. Telangiectasis of the thoracic skin overlying the attachment of the dia

phragm is commonly observed its significance is unknown (Burrett and Schorf AmJMSc 201 309 1941)

The dilated capillary can be occluded by use of the electric needle (Guequierre ADS 44 259 1941)

**Naevus Araneus** ( **Spider Nevus** ) is a common type of vascular dilation consisting of a central tumor of minute size with numerous capillary radiations. The little growths are usually solitary or few in number but they may be numerous, involving the face trunk, and limbs. Rarely they are pulsatile being communicant with arterioles.

**Papillary Varices (DeMorgan Spots Cayenne Pepper Spots)** are ruby colored, pinhead to pea size rounded vascular tumo s which develop especially on the trunk of middle-aged or elderly persons. Statistic study of them by Murison et al. (BMJ 1: 63 1947) revealed that the incidence rises with age from 5 per cent in adolescence to 73 per cent in individuals of 70 years; there was no relationship with malignancy

**Symptomatic Telangiectasia.**—Erythema ab igne may produce this, such as seen in stokers of coke ovens Lesions often appear dur g the 5th or 6th month of preg nancy and may disappear slowly after parturition (Davis JObGBE 45 667 1938) We have seen them appear following the ingestion of large amounts of vitamin D con centrates and carotinoid ich substances. They may sometimes represent the result of damage t capillary walls by circulating lipid substances such as 17 ketosteroids in preg nancy and the hyperlipemia of alcoholism and hepatic cirrhosis (Walsh ADS 47: 453, 1943 Bean: AmJMSc 204: 251 1942 AmHJ 25 463 1943) Telangiecta ia may represent in some cases a forme fruste of naevus flammeus localized or systematized and even affecting the meninges and central nervous system although such lesions present at or soon after birth tend t disappear spontaneously w thin 2 years. Weber (MP&Circ 10 *19 1943) discussed the varieties of tela giectasi including ruby spots branch ing linear varices of lower extremities, Osler s disease volar erythema, congenital vari cosities, hemangiectatic hypertrophy of the limbs (elephantiasis telangiectodes) the relation to purpura, telangiectasia macularis eruptiva persta s and it relation to urti caria and urticaria pigme tosa metastatic carcinoma and angioma serpiginosum.

Cutaneous arterial spiders were clearly distinguished from telangiectases by Bean (Med 24 43 1943) in a monographic article in which the relationship of estrogen and hepatic d sease to spiders and palma erythema was elucidated. I cirrhosis of th liver d minution of steroid metabol sm result in increased estrogen levels, and these result in spiders thought Lloyd and Williams (AmM 4 315, 1949) See also t langiec tasia macularis erupt va perstans, p. 399 a d erythema palmare p. 367

**Capillary Varices** f the lips are common. Circular smooth, purplish in color situated immediately beneath the epidermis generally of th lower lip, these soft com pressibl lesions are benign and pers stent.

**Hereditary Hemorrhagic Telangiectasis (Osler s Disease)** I an inherited anomaly affecting either sex The les ons appear at puberty Telangiectases and angiomas oc cur on the face tongue na al septum buccal mucosae and elsewhere including even the internal organs. R pture of these red or purplish vascular dilations may give rise to hemorrhage which may even require transfusions (Stellar NEngJM 226: 334, 194 ) Transmission by either sex (Goldstein AIntM 48 836, 1931) and as un usually large sibsh p was reviewed by Alban (NoWM 40 86 1941) in obving 6 generations Pardo Costello and Fariña (ADS 39 1023 1939) confirmed the histologic finding of elastic tissue deficiency Gastrointestinal and nasal bleeding was controlled by the admin stration f rutin 40 mg. t.i.d. by mouth by Koshlan (Gastroenterol. 7: 199 1946 Edit. J 133 47 194 ) See Osler (BullJHH 12: 333, 1901) Williams (ADS 14 1 1926) laid to rest the misapprehension that the condition is rare

## HEMANGIOMA

**Symptoms.**—A hemangioma is a localized hyperplasia of blood vascular tissue The lesions may involve the dermis the subcutaneous tissue or both They range greatly in size but are usually reddish or purplish in color with a flattened surface slightly elevated above the niveau Vascular nevi may be separated into 2 groups (1) flat or slightly elevated tumors composed of a superficial plexus of dilated capillaries angioma simplex, naevus flammeus, port wine stain and (2) bulky cystic angiomas hemangioma cavernosum



Fig. 806.



Fig. 807

Fig. 806.—Hemangioma macula nd papula purplish stain.
Fig. 807.—Cavernous hemangioma in infant.



Fig. 808



Fig. 809.

Fig. 808.—Macular hemangioma, "port wine" mark. Irremediable.

Fig. 809.—Typical scar of ca ernous hemangioma obliterated by -ray therapy during infancy 10 years previously) as good a result as may be expected.

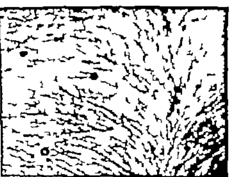


Fig. 810.



Fig. 811



Fig. 812.



Fig. 813.

Fig. 810.—"Cayenne pepper" angioma, abdomen.
Fig. 811.—Capillary hemangioma, vessels in dermis. (Dr. Fred Weidman.)
Fig. 812.—Angioma serpiginosum involving the thigh of a boy.
Fig. 813.—Progressive cavernous hemangioma; radioresistant, histologically benign, of 20 years' duration.

Hemangiomas are congenital or appear shortly after birth. They range in diameter from a millimeter to many centimeters. The lesions may appear anywhere. The port wine mark is common and may involve large areas shaped like areas of sympathetic nerve distribution. It does not undergo spontaneous involution.

NAEVUS FLAMMEUS NUCHAE is one of the commonest congenital defects of the skin. Appearing at birth on the nape of the neck, it generally has its long axis vertical and is roughly symmetrical. It may be only faintly pink. The edges are lacy (Corson AmJMSc 187 121, 1934)

SUPERFICIAL FADING HEMANGIOMAS.—Diffuse, flat, pale red areas over the nape of the neck, occiput or abdomen are often seen at birth. The color is intensified when the child cries. This type usually regresses spontaneously without treatment, more or less completely

CAVERNOUS HEMANGIOMAS develop slowly and may cause serious alteration, hypertrophy or destruction of the tissues by altering the blood supply They may be small at birth and gradually increase to a certain size where they remain stationary or spontaneously undergo involution, leaving white or mottled atrophic scars. One cannot predict which lesions will disappear Purplish, soft and compressible, they bulge when the child exerts himself and may rupture if ulcerated so as to bleed dangerously Large cavernous tumors are sometimes built about arteriovenous aneurism, and are audible (Seeger Surg 3: 264 1938) Multiple cavernous hemangiomas may be disseminated and are sometimes systematized. Other structures may be greatly altered by the presence of the vascular tumor so that elephantiasic deformity exists.

**Nervous System Involvement.**—Widespread involvement of the face is associated with like involvement of the meninges, and the ciliary body may be affected so that glaucoma results (Dunphy: AmJOphth 18: 709 1935 Goldberg ADS 53: 503, 1946) Spontaneous intracranial hemorrhage has been noted in association with trigeminal nevi (Cushing: J 47 178, 1906) Nevoid amentia is a name applicable to a syndrome of cavernous nevus in the fifth nerve distribution, vascular buphthalmos of the eye on that side, angioma of the pia and homolateral cerebral hypoplasia of the cerebrum, with atrophy and calcification (*Sturge-Weber disease*) See Mumsey and Miller (BMJ 1: 822, 1939) Anderson (YaleJBiol 18 103 1945) Contralateral Jacksonian epilepsy and hemiparesis commonly accompany the mental retardation in such cases.

**Venous Varix** of the neck is a simple blood cyst attached to a vein, and it appears clinically as a purplish tumor which expands with effort and is compressible.

**Angioma Serpiginosum** is characterized by multiple telangiectases which may start from a congenital vascular nevus but which often arise spontaneously The primary lesion is a small reddish angiomatous punctum. Extension occurs by the appearance of satellite lesions, which coalesce to form large patches. *The health of the patient is unaffected.* The disease slowly extends, with a tendency to fade in the center See Montgomery and Bailey (BJD 47 456, 1935 Wigley (Ib. 58: 66 1946) Hutchinson (ASurg 11: pt. 9 1890)

**Metastasizing Hemangioma.**—Robinson and Castleman (AnnSurg 104 453, 1936) found 4 cases in the literature like the one they reported. Theirs began in the breast *of a girl of 18 years.* While the histologic picture looked benign, the tumor behaved as though it were malignant. These tumors are radioresistant.

**Endothelioma** is a proliferation of lymphatic or blood vascular endothelium. Few authentic cases have occurred in the skin according to Sweitzer and Winer (ADS 34: 997 1936) who found only 6, 3 of which were suggestively associated with trauma. The lesions are *of* pea to orange size, dark red, fairly soft and may or may not have satellite nodules. They often ulcerate and may bleed profusely but are not painful as a rule. The microscope reveals the construction from capillary and capillary forming material. The lesions may be benign or of local malignancy Malignant angioblastomas are with difficulty distinguished from reticuloendothelial blastomas. See Sweeney et al. (ADS 50: 426, 1944); Caro and Stubenrauch (Ib. 51 295, 1945) scalp cases, radioresistant; Schwartz (APed 62: 1, 1945) malignancy disseminated in infant.

**Anemic Nevus** is characterized by vitiligo-like areas, occurring singly or in groups, and differing from normal skin only in vascularity The lesions are generally rounded in shape, their borders being sharply outlined and irregular like the borders of the nevi nuchal hemangioma. The surrounding skin is normal. The spots are made more apparent by friction, heat or cold or light cupping. Difference from vitiligo lies in the fact that there is no lack of melanin pigmentation. The lesion is white because of lack of blood vessels and without textural change (Piorkowski ADS 50: 374 1944) It can occur as a linear systematized abnormality (Pace: ADS 44: 944, 1941)

**Etiology and Pathology**—The cause of nevi is not known. The myth of prenatal maternal impressions has long been in the discard. Ribbert by injecting the vessels, showed that they have few or no lateral anastomoses injected material flows freely through the efferent and afferent channels. Yamada (JapJD 40 109 1936) discovered that hemangioma tissue does not wheal with histamine, and he believed that this indicates local aplasia of vasoconstrictor nerves. Histologically hemangiomas are growths made up of dilated capillaries, endothelium and connective tissue. The endothelium is closely packed and, in parts, solid and without channels

**Treatment.**—The earlier treatment is undertaken, the better (Bailey and Kiskadden Radiol. 38 552, 1942) The lesions sometimes undergo spontaneous obliteration, so that Anderson (JPed 25 148 1944) would not treat them until after the age of 5 years believing that they always stop growing by 1 year of age. On involution, spontaneous or forced, the result is cicatricial resembling the scar of a scald, and is usually hairless. Parents should be so advised before treatment is undertaken.

The treatment of hemangiomas in infants carries with it onerous medicolegal responsibility and is not to be entered into lightly

The electric needle serves for eradication of small capillary growths. Some lesions can be coagulated beautifully by means of solid carbon dioxide (Wrong CanadMAJ 41 571 1929) In deeply seated nevi resort must often be had to surgery The cautious use of filtered x rays is followed by flattening and blanching of the tumor It is generally agreed that small doses of radium or x rays (100 to 200 r ) at intervals of several weeks constitute the best plan (Andrews ADS 37 573 1938) In macular lesions, if the color does not disappear on diascopy it will not under radiation therapy Kaessler (J 110 1644, 1938) reviewed the injection of sclerosing agents as the means of treatment and Watson and McCarthy (SGO 71 569 1940) discussed treatment methods of all kinds. Port wine stains cannot be treated successfully as a rule, and in general should not be tampered with although they may perhaps be hidden by tattooing (see p 594) and can be concealed by certain cosmetic preparations. Jonsson (abs YBD 1947 p 133) described a method which seems promising: under Novocain anesthesia he rubbed off the superficies of the lesion with sterilized sandpaper and controlled bleeding with pressure bandages. We are tempted to try this it might work well

## ANGIOKERATOMA

This disorder usually limited to the extremities, is characterized by telangiectases and the formation of warty nodules enclosing dilated capillaries (" Telangiectatic Warts ") Several types of angiokeratoma are recognizable: (1) Mibelli's type; ( ) atypical, symptomatic forms, angiokeratosum or kerato-angioma; (3) hyperkeratosis in punctiform angioma, as of the scrotum; (4) hyperkeratosis in cayenne pepper spots; (5) angiokeratoma in a vascular nevus (6) angiokeratoma on the basis of postnatal telangiectasia; and ( ) transitional forms, similar t changes occurring in varicose veins (Wile and Belote: ADS 18 501 1928)

**Angiokeratoma (Mibelli).**—The lesions range from hempseed to pinhead size. They are distributed on the dorsal surfaces of the fingers and toes along the superficial capillaries, which are wider and more prominent than usual. Histologically, there are rounded lacunar spaces in the epidermis and these possess a regularly organized lining. Some spaces are partially or completely divided into compartments by thin septa, and most of them are filled with serum or coagulated blood. Chronic inflammatory changes occur in the papillary and subpapillary layers. The papillae near the lesions are hypertrophied. The horny layer is greatly thickened. The disorder occurs in individuals of chilblain circulation, and the lesions are usually more pronounced during the colder months of the year.

**Angiokeratoma (Fordyce).**—Forming a group of cases of a type distinct from that of Mibelli are those of Fordyce (Jour. Cut. Dis. 14: 81, 1896) in whose patient the lesions were small, discrete, asymptomatic reddish or purplish papules scattered over the scrotum. In many of such cases the tongue shows beneath it and along its border the telangiectases which characterize Osler's disease (Sutton: ADS 55: 348, 194). They are readily destroyed by high frequency coagulation.

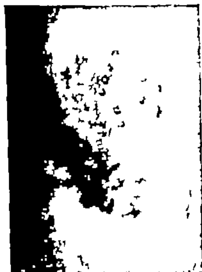


Fig. 814.



Fig. 815.

Fig. 814.—Angiokeratoma, patellar region. (Dr. R. N. Andrade.)
Fig. 815.—Angiokeratoma. (Dr. Fred Weidman.)

**Etiology and Pathology.**—The cause is unknown. Circulatory weakness, as evidenced by varicocele, varicose veins or a tendency to the development of chilblains, constitutes a predisposing factor. Liver disease is present in some cases. The change is probably primarily an injury of the blood vessel, resulting in subepithelial and intraepithelial hemorrhage, endothelial proliferation, fragmentation and loss of elastica, and perivascular inflammation. From verruca vulgaris the lesions are differentiated by the presence of dilated blood vessels. See Telangiectases, p. 590.

**Treatment.**—High frequency coagulation is effective.

## LYMPHANGIOMA

**Lymphangiectasis.**—Simple dilation, with or without vesicle formation, may involve either the superficial or the deep lymphatics. Superficial lesions appear as several whitish or pinkish, pinhead to pea size vesicles which may be discrete but are usually grouped, and which exude lymph when punctured. They are soft and compressible but their coverings are tough and elastic.

**Lymphangioma Circumscriptum** is characterized by a localized eruption of frog spawn like vesicles. The groups are generally few, from 1 to 3 in number, and the sit

of predilection are the thighs, upper arms, genitalia, and mucous membrane of the mouth. Early lesions are small, deeply seated opalescent vesicles. Later they may become thick, rough, and crusted, or even verrucose. When punctured, however the surprising quantity of milky lymphatic exudate discloses their nature. The lesions develop early in life, and are usually persistent. They give rise to no symptoms. Lymphangiomas of this type occasionally involve the tongue giving rise to macroglossia (Stokes: ADS 8 498, 1933)

**Prognosis.**—The lesions behave as benign tumors with rare exceptions.

**Treatment.**—Good results have followed the use of radiotherapy although the lesions are fairly resistant. They may be removed by excision, or electric cauterization, but they often recur Gant (ADS 64 202, 1946) used solid $CO_2$ with a good result.



Fig 816.



Fig 817

Fig. 816.—Lymphangioma circumscriptum involving neck.

Fig. 817.—Lymphangiectasis of thigh and mons due to inguinal tuberculous adenitis. (Dr F Ronchese)





Figs. 818 and 819.—Cystic lymphangioma hygroma. (Gross and Goeringer: SGO 69 48, 1939)

## KELOID

**Symptoms.**—A keloid is a dense fibrous growth which develops in mesodermal tissue, usually at the site of a scar and which is characteristically a smooth, firm reddish scarlike tumor Keloids develop gradually the first appreciable lesion generally being a deeply seated, firm, reddish, dome-shaped nodule, the surface of which is traversed by minute tortuous capillaries After attaining a certain size they may remain stationary or



Fig. 420.—Keloid following burn.



Fig. 421.



Fig. 422.

Fig. 421.—Keloid from piercing lobe. (Hall, T B [illegible] 32 376, 1938.)
Fig. 422.—Keloid at sites of acne lesions in Negro



Fig. 423.



Fig. 424.

Fig. 423.—Nuchal keloid, acne cheloidalis (Dr Clyde Cummer.)
Fig. 424.—Keloid, histologic structure. (Dr Fred Weidman.)

perhaps rarely undergo partial or complete involution. Ulceration is exceptional but it does occur The lesions are sometimes the source of spontaneous pain.

**Etiology**—Predisposition is a strong etiologic factor There exists a familial tendency to the disorder Negroes are especially susceptible Analogies exist between keloid and xanthoma, and their common occurrence in acne 12 per cent according to Garb and Stone (AmJSurg 58 315 1942) suggests a hormonal relationship The growths are composed of extremely large homogeneous fibers, interspersed with a few connective tissue cells having small, intensely staining nuclei The skin glands and hair follicles are pushed aside See atomic energy injuries, p 73

**Treatment.**—Only x rays, radium surgery and refrigeration are satisfactory In attacking extensive growths, x rays, 200 r each 3 weeks for perhaps 8 doses or less, are effective. Radium is valuable in keloids of small size Some authors have obtained admirable results from excision followed by radiation in erythema doses (Nason NEngJM 226 883 1942) Young, soft fast growing small keloids respond especially favorably old, large stationary hard growths are recalcitrant. Mere excision is generally followed by recurrence.

## NODULAR SUBEPIDERMAL FIBROSIS (HISTIOCYTOMA)

Hard fibromas are firm, reddish yellow nodules set in the dermis, the smooth surface usually rising slightly above the general level sometimes being depressed somewhat below it They begin as small infiltrations which enlarge to a diameter of about 1 cm reaching this stage of development,

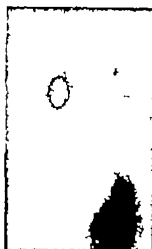


Fig 825



Fig 826

Fig. 825 —Histiocytoma over scapula, uncommonly large
Fig 826 —Nodular subepidermal fibrosis, histology

they remain unchanged over a long period of time They are hard, sharply defined, little tumors which may occur on the trunk or extremities of either sex at any age (Michelson ADS 27 812, 1933 Senear and Caro ib. 33: 209 1936) The lesions are probably not neoplastic in the blastoma sense but consist of adventitial cells frequently laden with lipid occurring with suggestive frequency in persons whose families contain diabetic sibs (Arnold

and Tilden ADS 47 498, 1943) Pathologically they range from small scarlike fibrous nodules with few capillaries, no pigment, no lipid, and no histiocytes, to highly vascular lesions with numerous phagocytes filled with hemosiderin and lipid stated Stout (JMoSMA 44 595 1947) who called them fibrous xanthomas and disagreed with Gross and Wolbach (AmJPath 19 533 1943) who thought them sclerosing hemangiomas.

**Hemosiderinotic Pigmented Histiocytoma (Pseudomelanoma).**—Histiocytoma may follow a minute hemorrhagic injury and the fixation of the blood pigment within it results in purplish brown pigmentation of the tumor which clinically bears close resemblance to malignant melanoma. In the cells, the Prussian blue microchemical test shows the pigment granules to be iron-containing melanin is iron free (Bernstein ADS 40: 390 1939) Blue nevus is to be distinguished.

**Treatment.**—Excision must be wide to prevent recurrence. Recurrence in a scar resembles keloid. A single dose of 1200 r at 100 kv no filter added is likely to be curative No treatment is essential for the lesions are harmless.

## PAINFUL NODULE OF THE EAR

Chondrodermatitis nodularis chronica helicis is manifested as a small, nodular painful benign growth occurring on the rim of the ear The growths appear suddenly without history of previous injury They are solitary from 3 to 4 mm. in diameter embedded in the skin, usually unattached to the cartilage. After reaching a certain size, they remain unchanged for years. Excision cures. See Poth (TexasSJM 33 19 1937)



Fig. 327



Fig. 328.

Fig. 327.—Painful nodule of the helix.
Fig. 328.—Subungual exostosis, great toe (Dr [illegible])

## SUBUNGUAL EXOSTOSES

Small, solitary, nodular benign bony anomalies are occasionally seen, developing generally from the medial aspect of the terminal phalanx of the great toe in young adults. The lesion, a smooth bulging one as a rule, gives symptoms only because it is pressed by the confinement of shoe [illegible] corn may develop on its glazed firm surface.

X-ray examination reveals a pedunculated, rounded nodule of bone attached to the phalanx. Clinically it may be mistaken for ingrowing nail, fibroma or malignancy. The treatment is complete removal. See Shaffer (ADS 24: 371 1934)

## OSTEOMA OF THE SKIN

True bony deposits in the skin are exceedingly rare. Their nature is seldom recognized until the tissue has been examined microscopically. The lesions may be single or multiple. They are round, sharply defined, and hard. Shotty papules in a woman's face probably represented ossification of milia, reported by Cannon (ADS 53: 708 1946). Ossification may develop in laparotomy and other scars. Cutaneous metastasis of ossifying sarcoma has been seen. See also calcifying epithelioma and calcinosis. Excision is the only suitable method of treatment. See Becker (ADS 10: 163, 1924); Vero et al. (J 129: 728, 1945)



Fig. 829.



Fig. 830.

Fig. 829.—Osteomas, congenital. (Vero et al. J 129: 728, 1945.)
Fig. 830.—Osteoma, histology. (Vero et al. J 129: 728, 1945.)

## LIPOMA

Dermal or subcutaneous new growths are seen composed of fat cells enclosed within a capsule of connective tissue. They are spheroidal or lobulated and exhibit great range in size. The growths consist of irregularly large adipose lobules, thinly encapsulated in fibrous envelopes, the septa of which carry the nutrient vessels but lipomas may be infiltrative in character with fine tongues of fatty tissue projecting outward along the blood vessels and between the muscle bundles. Increase in size is usually gradual. The tumors are freely movable. They seldom give rise to symptoms. They are almost always benign but liposarcoma is known (Stout AnnSurg 119: 86 1944). Familial occurrence has been noted. They generally make their appearance at middle age and occur in order of frequency in the regions of the shoulder, back, neck, arm, forearm, axilla and thigh (Hogue WestJSGO 50: 332 1942). Weber (MP&Circ 209: 203, 1943) provided an interesting review of lipomatoid dysplasias of the subcutaneous tissues.

In the epigastric region small hernias often strongly resemble lipomas. Lipoma like lesions may develop at the site of injections of insulin (see dermatitis medicamentosa)

Treatment.—Enucleation is the only successful plan, care being taken to remove all of the fatty tissue and its capsule. Generally lipomas may be neglected. If sarcoma is suspected, excision must be wide.



Fig. 131 —Lipoma. (Dr Hartzler)

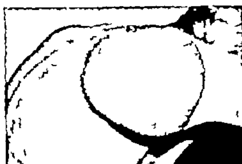


Fig. 132.—Lipoma, unusually large.

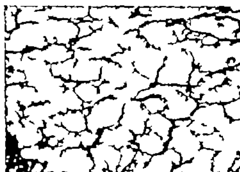


Fig. 133.—Lipoma, histologic structure.

Liposarcoma is divided by Stout (JMoSMA 44 656, 1947) into 3 groups. The first is myxoid and slimy on gross section, with areas of embryonal yellow fat if the tumor remains well differentiated; it does not metastasize, but it frequently recurs if incompletely removed. The second shows rounded cells without mucin, some cells being of spindle shape as in fibrosarcoma. The tumor resembles embryonic brown fat, and the lesion is malignant. The third type consists of tumors combining the elements of the first two and is fully malignant. Liposarcoma is the second most common soft sarcoma. It is found in the thigh and retroperitoneal tissues in persons of later years. Sixty per cent of Stout's patients have been past 40. Sometimes the lesions are huge one on record weighed 275 pounds. Wide removal or amputation is indicated.

Adiposis Dolorosa, a lipoma-like disorder is characterized by irregular and painful deposits of fat in the subcutaneous tissue of the trunk and limbs. The incidence is 5 times as frequent in women as in men (Wilson: AmJSurg 19 485, 1933) and the age is generally between 45 and 60 years. The skin is often dry and harsh, and pituitary and other endocrine changes have been found. Three types have been described (1) the nodular which is rare; (2) the circumscribed and disseminated, which is commonest; and (3) the generalized and diffuse type. The tumors are slow in development, usually elevated and sometimes reddish or bluish in color. Their painfulness is generally slight on pressure but great when spontaneous. The distribution is usually symmetric, and the legs, thighs, and trunk are especially affected. Injections of from 10 to 60 c.c. of 0.2 per cent procaine into the hardened fat may give relief.

## ENDOMETRIOMA

Endometrioma is a tumor composed of dense fibrous tissue smooth muscle and adenoid structures. It may exceptionally occur at the umbilicus. Cysts in such lesions lined with cylindric epithelium, are filled with material of chocolate color derived from blood. The occurrence of a menstruating tumor at the umbilicus in women 33 to 35 years of age, and its swelling, pain, and perhaps bleeding at menstrual periods are unique features. The lesions can result from implantation in laparotomy scars.

CULLEN'S SIGN.—A purpuric stain appearing at the umbilicus is so designated. It signifies subperitoneal hemorrhage, generally the result of ectopic pregnancy.

The umbilicus is subject to many abnormalities of dermatologic interest including cysts originating from urachus or allantois, allantoic polypi, dermoid cysts, and concretions, as well as angioma, verruca, granuloma pyogenicum, and other skin tumors. See Cullen (The Umbilicus, Saunders, 1916).

## MYOMA

**Leiomyoma.**—Tumors composed of smooth muscle fibers occur in the skin and subcutaneous tissues. They may be solitary or multiple and when multiple they may be grouped or unilaterally systematized. Solitary tumors were well described by Stout (AmJCa 24 255 193 ) who commented that glomus tumors are not the only subcutaneous painful ones. There was no predilection as to sex, age or race. The locations of preference were the extensor surfaces of the extremities, nipple region, scrotum, labia majora, and sides of the face. The lesions are usually small, round and nodular elevating the superjacent skin, encapsulated and freely movable. Injection of epinephrine increases the pain. In one patient the tumor doubled in size during pregnancy. Histologically Stout found types, those with and those without association with blood vessels. Cajal staining reveals delicate neurites possibly connected to the smooth muscle fibers but not sensory. The lesions are benign, and are cured by excision. Diagnosis depends on histologic examination. See Ormsby (ADS 11 466 1925).





Figs 334 and 335.—Leiomyoma. (Dr Kendall Frost.)

**Myosarcoma (Rhabdomyosarcoma)** is a lesion rarely encountered in dermatology. It occurs in the tongue (Klemperer AmJCa 20 324 1934) as a comparatively benign, slow growing tumor surmounted by proliferating epithelium so as to resemble a carcinoma, well delimited but seldom truly encapsulated, and identifiable by the ribbonlike syncytial masses and large polygonal cells with granular cytoplasm but no striations. Mitoses are rare. Three cases involving the skin of the trunk and manifested by a xanthomatic nodules of 1 to 2 cm. in diameter were described by Tate and Schmidt (ADS 40 223 193 ) who noted the xanthoma-like cells and multinucleated strands between the connective tissue bundles of the cutis. While most cases occur in

adults, those involving the alveolar processes occur chiefly in children (Bloom and Gloder: ADS 56: 648, 1947) Cipollaro and Einhorn (ADS 56: 812, 1947) reported 2 cases and reviewed 164 found in the literature 62 of which were lingual, 18 from the skin, 17 subcutaneous, 13 intramuscular 11 maxillary 8 laryngeal, 8 mammary, 6 mandibular 4 labial, 3 from the ear and 14 from other locations. Malignancy is low and metastasis has been observed in only a few cases. Excision is curative See Stout (AmJCa 34: 31 1938)

## GLOMUS TUMOR

Special organs of arteriovenous anastomosis, the Sucquet Hoyer canals are found in many parts of the body but are most numerous in the tips of the fingers and toes. Occasionally one of these structures undergoes benign neoplastic change resulting in the formation of a tumor The lesions, occurring by predilection on the extremities, the fingers and even beneath the na l, are small, rounded pinki h or purplish, fleshy



Figs. 616 and 617.—Glomus tumor gen appearance. (Lewis and Geschickter J 103 776, 1935.)



Figs. 618 and 619.—Glomus tumor from child' penis, ubependermal elements, and glomus cells adjacent t capillaries (Grauer and Burt J 112 1806 1938.)

nodules, composed f convoluted vascula hannels surrounded by smooth muscle cells, among which nerve filaments are interw ned The epithelioid cells have been cultivated in vitro, manifesting a discrete habit small cell body and many branching processes, so that they are considered t be pericytes by Murray and Stout (AmJPath 18 183, 1942) The tumors occu wher pericytes are found and they may occur in places where glomera are not found. They are remarkable in givi g rise to iolent and excruciating pain paroxysmally on manipulation or trauma Th develop in size only to a certain point then remain stationary (Weidman and Wise ADS 35: 414, 1937) Kaufman nd Clark (AnnSurg 114 1102 1941) reported 4 cases occurring in one family Love (PrMMC 19 113, 1944) stressed the fact that pinpoint pressure elicits pain at an exact spot and does not do so 1 cm. distant Excision curative

Painful nodules (tubercula dolorosa) w re discussed by Stout (AmJCa 36 25, 1939) spontaneous pai being sometimes observed not onl in glomus tumors but also in leiomyomas, fibromas, neurofibromas, fibrosarcomas, keloids, and dermoid cysts.

## NEUROMA

New growths consisting of nerve tissues are extremely rare. The lesions are discrete, sharply defined, pea size tumors which are firm and elastic to the touch. They generally become sensitive, and occasionally they are the seat of violent paroxysmal pain. Neuroma is to be differentiated from leiomyoma, fibroma, and glomus tumor by histologic findings. The tumors are benign. They should be excised, or the nerve which supplies them resected. Monographic is the article on nerve tumors by Foot (APath 30 772, 808, 1940)

**Amputation Neuroma.**—When nerve fibers are cut, degeneration is followed by outgrowth of filaments through the nerve sheaths, and an intertwined mass results if obstruction is met at the terminus. Such lesions account for the tender points and paresthesias usual in scars.

**Ganglioneuroma.**—Montgomery and O'Leary (ADS 29 26, 1934) reported a rare papular and nodular eruption in a 26-year-old male. The discrete round, firm, yellowish lesions varied from 1 mm. to 1 cm. in diameter They appeared first over the buttocks and spread to the pubes, abdomen, axilla, back, and neck, with a small scattering elsewhere. Histologically they found in the early nodules large, palely staining cells with features of sympathetic ganglion cells.

## PILOSEBACEOUS ADENOMAS

***Adenoma Sebaceum.***—*The lesions are of pinhead to split pea size* yellowish in color and usually distributed in a symmetric manner over the nose, cheeks and nasolabial folds (Gilman ADS 35 633 1937) They are long benign but persist indefinitely and they sometimes develop into basal-cell carcinomas. Familial incidence is often noted. Adenoma sebaceum is sometimes associated with tuberose sclerosis, mental deficiency and convulsions (Noon and Williams ADS 50 96 1944) Pringle's syndrome (BJD 2 1 1890) comprises the combination of these lesions with subungual and periungual warty fibromas. The relationship of tuberose sclerosis with adenoma sebaceum is not mere coincidence. Formes frustes are seen, and epiloia may be associated with other ectodermoses such as neurinomas, neurofibromas, nevi, pigmented spots, and the like (Butterworth and Wilson ADS 43 1, 1941) See review of Woolhandler and Becker (ADS 45 734 1942) Adenoma sebaceum of Pringle was clearly distinguished from epithelioma adenoides cysticum of Balzer by Artom and Cerruti (abs YBD 1946 p 297) The lesions of the former are smaller vascularized, soft and fleshy centrally located on the face associated with other nevi and with formes frustes of v Recklinghausen's disease, rarely familial histologically constructed of vessel and connective tissue hypertrophy sometimes containing sebaceous glands, and never undergoing malignant degeneration The latter are larger whiter firmer irregularly located on the face and not associated with nevi or with central nervous system disease, are usually familial are constructed of epidermal adnexal tissue and commonly undergo basal-cell carcinomatous progression

**Epithelioma Adenoides Cysticum** is characterized by the occurrence of a few or several pinhead to pea size, rounded shining translucent nodules which exhibit a predilection for the face. They are of firm consistency and give rise to no symptoms. They are generally discrete, but may be closely bunched. Telangiectasis is an accompanying feature about large lesions A familial tendency is frequently noted. While usually numerous, solitary lesions are seen. They begin as tiny papules, which gradually develop up to a certain point where they remain stationary On the face the distribution is often more or less symmetric but on other parts of the body this tendency is absent. When malignancy supervenes, as it sometimes does, waxy nodules of basal-cell carcinoma develop, slowly progress and ulcerate with variations in rate of growth. See Traenkle

(ADS 42 822, 1940) Greenbaum and Shaffer (Ib 46 564 1942) It is probable that most basal cell carcinomas start as solitary accessory structure hamartomas of the epithelioma adenoides cysticum sort, remain benign for perhaps years, suffer trauma at the hands of the patient who mistakes them for comedones or milia, and then grow progressively

**Etiology and Pathology**—The lesions represent dysontogenesis of the hair apparatus. Women are affected more frequently than men. The lesions commonly become apparent about the age of puberty Histologically the papules are composed of organoid collections of basophile epidermal cells the arrangement of which parodies the pilosebaceous apparatus (Ingels ADS 32 76 1935)



Figs. 340 and 341.—Epithelioma adenoides cysticum, and histologic structure.

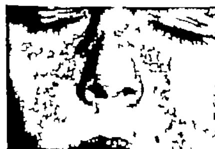


Fig. 342.

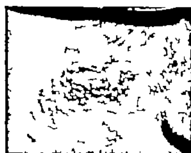


Fig. 343.

Fig. 342.—Epithelioma adenoides cysticum

Fig. 343.—Sebaceous naevus of cheek composed of hypertrophic fat glands.

**Treatment.**—Growing lesions should be destroyed. Excellent results follow the use of radium. Cauterization or skillful coagulation will likewise serve. The lesions are treated individually Scarring is unavoidable.

## SEBACEOUS CARCINOMA

Tumors of sebaceous glands are rare, excepting the benign lesions elsewhere described as hypertrophic fat gland and naevus sebaceus. A sebaceous carcinoma resembles a basal cell carcinoma in clinical appearance and behavior It is diagnosed by histologic examination, which reveals the unforgettable picture of sebaceous cells in

neoplastic arrangement and all stages of evolution. Cure is readily obtained by adequate surgical or x ray therapy. See Warren and Weed (AmJPath 19: 441 1943) Sweitzer (ADS 54: 583 1946) Lever (ADS 5 : 102, 1948)

## SYRINGOCYSTADENOMA

Benign, cystic epithelial tumors derived from coil gland elements are uncommon. Most cases have occurred in adult women. The lesions are small, yellowish or brownish, slightly elevated and soft and elastic. They develop slowly persist indefinitely, and give rise to no symptom. The sites of predilection are the axillae shoulders, and chest. They are often systematized, limited in distribution like a naevus unius lateris. The lesions represent dysontogenesis of the sweat apparatus. Homma and Escher (ADS 33: 700 1936) suggested that the tumors arise from apocrine sweat glands. Sections reveal malformed sweat tubule epithelium forming aimless coils in the connective tissue stroma of the dermis. Little cysts are formed and hyaline concretions are present in some of them. Roentgen therapy generally succeeds in eradicating the lesions. They may safely be neglected as a rule.



Fig. 844



Fig. 845.

Fig. 844.—Syringocystadenoma. (Dr. P. Schaffner.)
Fig. 845.—Syringocystadenoma.

**Syringoma (Hidradenoma)** is the name applicable to small, white circumscribed, elastic, innocent looking tumors which generally are solitary and located on or near the vulva. See McDonald (AmJClPath 11 890, 1941) Gates et al. (AmJPath 19 591 1943) Novak and Stevenson (AmJOG 30 641 1945) Cunningham and Hardy (SouthSurg 13 831 194 )

The gross section shows encapsulation of a white and adenoid bulging material, and the microscope discloses bizarre epithelium lined clefts suggestive of apocrine or sudoral organ. Eversion is curat. Compare naevus syringocystadenomatosus papilliferus. The myoepithelium of the sweat gland was thought to be the origin of 3 little tumors, one of which from the toe behaved like a malignant melanoma, described by Sheldon (AJPath 41 726, 1941)

**Cylindromas** ... neoplasms of local activity only. They arise probably from pilosebaceous and sudoral anlagen and progress to form smooth rounded nodules of pea to walnut size. Groups of such nodules are of more common occurrence than their solitary appearance. Their situation on the scalp gives rise to a condition described as turban tumor. T le t m rs re not al y f the same struct re they may be tricho epitheliomas in some instances. Some think them variants of epitheliomas ade

adenoides cysticum. See Ronchese (AmJCa 18 875, 1933) Binkley (ADS 37 239 1938) We (ADS 30: 193 1934) described a case of cylindroma of the typical syringomatous, not trichoepitheliomatous, type, attributing the nodules to proliferation of sheath cells of sweat tubules these cells Lever (ADS 57: 332 1948) judged to be myoepithelial, and for such tumors he recommended the name myoepithelioma. In treatment they may be excised. They do not metastasize.



Fig. 846.

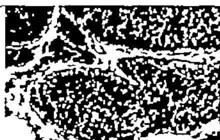


Fig. 847

Fig 846.—"Turban tumor" cylindroma. (Dr F Ronchese)
Fig. 847.—Cylindroma, histologic structure. (Dr F Ronchese.)





Fig 848.—Nodular syringoma involving the neck, unilaterally. Lesions on cheek are nevus cell tumors. Photomicrographs show above an isolated sweat gland lobule overlying one nodule representative of syringoma; below small, dark-staining, presumably myoepithelial cells surround a central dermoid tubule (ADS 36 105, 1934.)

## CONGENITAL DERMAL FISTULAS AND SINUSES

There are several sites on the surface of the body where improper embryologic development results in incomplete closure of a fold or invagination, or incomplete resorption of an epithelial tract. Lesions of this origin include branchial cleft cysts and sinuses, sacral and coccygeal cysts and fistulas. Failure of closure results in fistula formation, partial closure in cystic lesions, incompletion in dimpling, these manifestations representing various degrees of defect. See Anderson (J 135 607 1947)



Fig. 849. Fig. 850

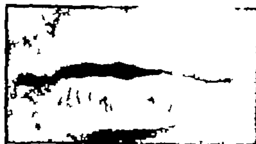


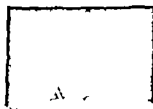
Fig. 851. Fig. 852.

Figs. 849 and 850.—Congenital auricular fistulas. (Becker ADS 46: 520 1942.)
Figs. 851 and 852.—Secondary infection of congenital auricular fistulas. (Pastor and Erich AOtol 36 120, 1942.)



Figs. 853 and 854.—Congenital fistulas, longitudinal and cross sections (Drs. Becker and Pastor and Erich.)





Figs. 855 and 856.—Congenital fistula of lower lip Roentgenogram of wires in fistulas. (Ladd and Shirazy InternatCli 3 71, 1938.)

**Congenital Auricular Fistula** occurs as a tract with its orifice marked by a shallow depression just anterior to the ascending limb of the helix above the tragus. The depth is variable, and may extend even to communication with the middle ear or nasopharynx. The lesions are not rare. Irregular periods of infection and inflammation are usually the occasion for their discovery. Cyst formation occurs, and dermoid cysts are found here sometimes (Pastore and Erich: AOTol 36: 120, 1942). See Becker and Brunschwig (AmJSurg 24: 174, 1934); Selkirk (AmJDisChild 49: 431, 1935); Becker (ADS 48: 520, 1943).

**Fistula of the Dorsum of the Nose.**—A pinpoint sinus, from which yellowish matter, hair, blood and watery fluid are from time to time discharged or squeezed, characterizes dermoid lesions of the dorsum of the nose. The sac is commonly of collar-button shape extending through the nasal bones. Infection is liable to complicate the lesions spontaneously or as a result of manipulation (Lamego: AOtol 18: 765, 1933).

**Congenital Fistula of the Lower Lip** may exist as a painless cosmetic defect sometimes associated with a deeply dimpled chin or with a dimple just beside the septum of the nose (Lody and Blurary: InternatClin 3: 75, 1939; Gurney: WestJSOG 48: 733, 1940).

**Pits of the Lips.**—Deep clefts on each side of the midline of the lower lip were described by Mason et al. (SGO 70: 12, 1940).

**Fistulas of the Labial Commissures** are symmetrically located in the angles of the mouth. The orifices are within the mucous surface of the labial commissures, and the canal, perhaps half a millimeter in diameter, extends laterally to a variable but shallow depth between the interlacing muscle fibers of the orbicularis oris. There occur in them mild infections, which may be treated successfully by applications of 10 per cent silver nitrate.

**Umbilical Fistula.**—Intermittent discharge from the umbilicus with attacks of pain and inflammation may be due to a sinus representing persistence of the urachus.

**Perianal Cysts.**—In the development of the caudal parts, complex changes involve the medullary tube, primitive gut, notochord, and cloaca. Cloacal vestiges found in the anorectal canal, giving rise to anal glands, are common sources of fistulas, fissures, and perirectal abscesses, as well as of caudal gut cysts and cloacal cysts.

**Pilonidal Cysts** are sometimes demarcated on the skin by the presence of a hairy pigmented mole, a dimple, or a crusted papule. Sinuses may open in the median line over the lower sacrum or coccyx. Sinuses in higher cord segments occur but are rare. They may even penetrate the meninges, and the symptoms of some cases include recurrent attacks of meningeal irritation or inflammation. The sinuses are lined with squamous epithelium. They extend upward in a sometimes erratic and difficultly discoverable course, even within the sacrococcygeal joint itself. They often contain hair in a terminal pocket an inch or two from the orifice. Cysts and abscesses readily occur. See Walker and Bucy (Brain 5: 401, 1934); Gage (AnnSurg 109: 291, 1939); Tendler (SMJ 34: 1166, 1941). Marks (SMJ 40: 844, 1947) described treatment by incising tracts, suturing their lining to skin.

**Perineal Fistula.**—Cysts or sinuses may occur along the perineal raphé from urinary meatus to anus. These may be mucous or dermoid, and are subject to infection with the gonococcus.

**Coccygeal Fistulas** are congenital defects occurring usually in the male, only in the white race, sometimes familial, and often in association with other developmental anomalies.

Treatment in all types of congenital sinuses is excision, which is sometimes quite difficult. Inconsequential lesions may be neglected, but all cystic ones ought to be removed in view of their potentiality for serving as the point of origin of carcinoma. In delineating the course and extent of sinuses and fistulae and the ramifications of cysts, which are by no means always simple, preoperative injection into the tract of methylene blue solution or roentgenologic study utilizing the injection of radiopaque substances, greatly clarifies the necessary surgical planning and work.

## CYSTS

Cysts are lesions which particularly justify the statement of Bland Sutton, "Many tumors become manifest by the accumulation of the products of their own activity." The following are of dermatologic interest.

**Milia** are small, dense sharply circumscribed noninflammatory elevations due to retention beneath the epidermis of material from occluded normal or rudimentary sebaceous glands. Often associated with comedones, milia differ in that the corneum covers the sebaceous content so that this sebaceous material is white being not oxidized black like the exposed surface of a blackhead. Sometimes milia are numerous and comedones are absent. The sites of predilection are the forehead, malar temporal and eyelid areas. All areas subject to acne may be affected. Milia of the lip are sometimes seen in Fordyce's disease. They are persistent but harmless. Picking at them with dirty instruments may lead to infection or scar. The presence of many milia usually signifies that the patient drinks a good deal of milk. The lesions on rare occasions undergo ossification (Costello ADS 56 536, 1947)

**Sebaceous Cysts** are to be distinguished from wens. They are derived from sebaceous glands usually by obstruction and are generally acquired rather than hamartomatous anomalies. A milium is a minute cyst occurring in a sebaceous follicle as a hard white, subepidermal object which can be picked out through a tiny slit made in the overlying tissue. Lesions intergradient between comedones, milia, and sebaceous cysts are commonplace. The larger the accumulation of sebum, which has a rancid butter odor the more obscure becomes the orifice representative of the sebaceous follicular mouth. When the opening does persist it is generally occluded by a blackened, oxidized plug of waxy material.

Histologically the tumors consist of encapsulated masses of epithelial cells in various stages of degeneration and disintegration and cholesterin crystals. The capsule composed of fibrous connective tissue is lined with stratified squamous epithelium which may be infiltrated with lipid matter. Inflammation involving these cysts and their capsules may be reaction to either lipid or bacteria or both.

**Steatomas (Wens)** are smooth globular pea to orange size or larger subcutaneous tumors which arise probably from hair anlagen. They are usually located on the scalp. A sebaceous cyst is by definition a cystic alteration of a sebaceous gland a wen is presumably a retention cyst (Love and Montgomery ADS 47 185, 1943). Atheromas and cholesteatomas are wenlike being filled with cholesterol crystals and similarly lined with stratified squamous epithelium.

The tumors may be solitary or multiple. They may be inflamed or quiescent. They commonly occur in middle age. Women are affected more frequently than men. Wens may develop into carcinomas. The tumors may reach enormous size and cause repulsive deformity. They may be inherited as a dominant sex linked to the female. Collins (CanadMAJ 35 370 1936) considered all cases precancerous, for 3 cases he reported and 64 he found in the literature were all cases in which squamous carcinoma had developed in such lesions of the scalp.

**Treatment** is surgical. The lesions can be eradicated by means of caustics, such as phenol or a bit of solid silver nitrate put into the sac after the contents have been squeezed out through a narrow incision (Shaw SoCarolMAJ 35 90 1939). An elliptical incision may be made following the margin of the lesion which is generally attached inextricably to the skin immediately overlying it. Subcuticular suture with 000 catgut can be used to avoid holes in the skin and to obtain minimal scarring. Removal of the cyst by dissection is facilitated by injecting Novocain intradermally at the top and continuing the injection until the

fluid has swelled the entire capsule establishing a line of cleavage. Dunna (NOrlMSJ 98 5 1945) inserts a sharp needle vertically just entering the cavity and applies monopolar diathermy via this electrode sufficient to induce a slough of about one-fourth the diameter of the cyst; in healing, the cyst wall contracts and becomes level with the epidermis (see J 135 320 1947)



Fig. 557



Fig. 558

Fig 557.—Wens ... ed, fortuitously alopecia ... eata. (Dr J P Quenelle)
Fig. 558.—Sebocystomatosis of scrotum.



Fig. 559.
Comedo-milium.



Fig. 560.—Milia
(Dr Stuart Way)



Fig. 561.
Synovial lesion

**Chalazions**, analogues of sebaceous cysts, develop in the eyelids from Meibomian glands.

**Sebocystomatosis (Hereditary Sebaceous Cysts; Steatocystoma Multiplex)** is an abnormality generally familial, in which a considerable number of atheromas are distributed over the body. The lesions are simple cysts, whitish, doughy and asymptomatic, though disfiguring (Sachs ADS 38 87 1938). The content is odorless, usually unoxidized, and possesses chemical properties intergradient between those of blood lipid and depot fat (Lynch and Fieber JIn D 8 63 1947). They may be limited in distribution to the scrotum, which then presents a curious appearance, studded with white nodules (Ronchese ADS 49 12 1944). Calcification of the content may take place.

**Dermoid Cysts.**—The lining of these cysts is stratified squamous epithelium, and accessory skin structures are present including sebaceous glands, hairs, sometimes coil

glands, and even teeth. Dermoid cysts should be excised. The danger of the origin tion of squamous carcinoma within them makes this urgently desirable (New and Erich: SGO 64: 48 1937 Erich: AmJSurg 50: 67 1940) Scalp cases are sometimes of collar button shape involving the diploe and giving rise to bone defects demonstrable by x-ray (Quade and Craig: PSMMC 14 459 1939)

**Traumatic Epithelial Cysts.**—It is possible for a bit of epidermis to become traumatically displaced to a position beneath the surface. There, its continuing to proliferate results in the development of a subcutaneous or intracutaneous, hard, round cystic tumor lined with stratified squamous epithelium, filled with horny debris and surrounded by a capsule of centrifugally displaced fibrous tissue. When epithelium proliferates in the absence of a free surface to grow upon, concentric corpuscles are formed; such were produced experimentally in Triturus by Kent (AnatRec 75: 275, 1939) Such lesions occur by predilection on the palmar surface of the hands and fingers, occasionally on the feet, and are aptly called implantation cysts. The typical implantation cyst is subcutaneous and of pinhead to cherry size. Slow enlargement and slight tenderness are the rule. There is usually a latent period intervening between the injury and the clinical appearance of the cyst, which may progress rapidly One must differentiate metastatic tumor synovial lesion, fibroma, xanthoma, ganglion, sebaceous cyst, atheroma, and dermoid cyst. Osteomyelitic cavities may acquire a partial or complete epithelial lining by the growth of epidermal tissue into the sinuses. Excision must be complete to cure. See Blasel and Brunschwig (J 108 1702, 1937) Cogswell and Goodale (JLCM 25 5 6, 1940) Dolce and Clark (NYSJM 44: 2353, 1944)

**Synovial Lesions of the Skin.**—Cystic lesions occur beneath the skin in the vicinity f joints, particularly on the dorsal aspect of the interphalangeal metacarpophalangeal, and metatarsophalangeal articulations. The surface is usually smooth and shiny The lesions contain ropy clear yellowish fluid. If opened they refill. The lesions are cysts, perhaps originating in synovial endothelium, o perhaps representing myxomatous degeneration of the dermis (Gross SGO 65 289 1937; Savatard: ADS 9: 441 1934) They are radiosensitive, requiring 3 or 3 doses of 500 r according to Woodburne (ADS 56 407 1947) but may alternatively be dissected out (MacKee and Andrews: ADS 5 561, 1922)

## CALCIFYING EPITHELIOMA

**Symptoms.**—Calcifying epitheliomas are slow growing, firm or hard, sharply encapsulated new growths. They occur on the head arms, forearms, and back in order of frequency in persons who may be young or in early adult life. The shape is spheroidally rounded. The size is from 1 to 3 or even 6 cm. in diameter The location is within the derma, fixed to the skin above and freely movable over the deeper tissues.

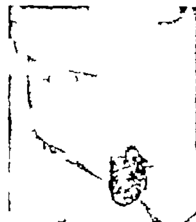


Fig. 442.



Fig. 443.

Fig. 442.—Calcifying epithelioma, producing horn
Fig. 443.—Calcifying epithelioma, histologic structure. (ADS 31 48, 1935.)

The gross section shows a gritty granular surface. They may ulcerate, crust, and build up a hornlike mass of coherent débris (Sutton and Sutton: ADS 31: 48, 1935)

Pathology.—Bands of stratified squamous epithelium are set in a dense, fibrotic stroma remarkable for the giant cells in its structure. Some of the epithelium is living and proliferating; some is decadent or dead and serves as foreign body substance rich in lipids. Cholesterol clefts are commonly found. The stroma is to be interpreted as foreign body reaction. Ossification often occurs (Highman and Ogden: APath 37: 169 1944)

Etiology.—The lesions may develop from wens or cystic tumors. They are usually clinically mistaken for cysts. A discontinuity in the wall of a cyst with epidermal lining, resulting from trauma or inflammation, allows foreign body reaction on the part of the mesodermal tissues to take place, while epithelium which previously lined the cyst simply continues to proliferate. See King (AmJP 23: 29 1947)

Treatment.—These tumors behave as benign neoplasms of local growth, amenable to local excision.

## SEBORRHEIC KERATOSIS

**Seborrheic Keratoses (Acanthotic Nevi Senile Warts)** begin as small, round, warty brownish, sharply circumscribed thickenings of the epidermis. Persons beyond middle age are usually the ones involved. The site of




Fig. 341.—Seborrheic keratoses. *A*, Typical lesions on the back; *B*, one type of structure, epidermal folds resting on elongated dermal papilla *C* another type of structure with large masses of anomalous epithelium.

predilection is the trunk, in contrast with the senile keratosis in its predilection for exposed surfaces. When fully developed the growths are flat topped papules or tumors, oval in outline, brownish or blackish in color sharply circumscribed, perhaps pedunculated and vegetative but usually sessile, and covered with an unctuous scale. They may be solitary few or many The tumors persist indefinitely with little growth. Occasionally the epithelium of which they are composed becomes proliferative and ear

cinomatous. The change, when it occurs, involves first a part of the lesion, and the process spreads. The lesion becomes vegetative, crusted, and malodorous the microscope reveals a papillomatous, medullary squamous carcinoma The tendency to malignant change, however is slight. Occasionally the lesions are quite itchy

**Pathology**—The microscope reveals acanthosis, the thickened epithelial layer being papillomatous to greater or less degree. The cells are ordinarily similar to the cells of basal cell epithelioma, being uniform, basophilic, fairly regular somewhat spindle shaped and palisaded along the dermo-epidermal junction which is unbroken. Dermal papillae are elongated and their vessels dilated. The acanthotic epithelium degenerates externally to form the greasy external material which covers the tumor Among and between the cells of the acanthotic epithelium are dendritic cells containing melanin granules. Some lesions contain much more pigment than others.

**Diagnosis.**—Senile keratoses and early epidermal carcinomas are distinguished by their harsh horny scale Melanotic nevi may closely simulate acanthotic nevus as a rule, true nevus has existed since early youth, while the keratosis is acquired at a later age See Eller and Ryan (ADS 22 1043 1930) *and Montgomery (MinnM 18 735 1935)*

**Prognosis.**—The large majority of the lesions are benign It would seem that basal-cell cancer pigmented basal-cell cancer and, perhaps, keratinizing carcinoma may occasionally originate in them They seem to be autoinoculable

**Treatment** consists in destructive removal of the cells which comprise the tumors. They should be treated individually Any physicotherapeutic agent which blisters can be used we prefer the actual cautery Accurate separation of epithelium from dermis may be accomplished and with gauze the steamed and loosened epithelium may be wiped away leaving a denuded but unharmed cutis The wound heals in from 7 to 14 days, and little scar results. Radium or x rays in unfiltered dosage for superficial peeling effect will accomplish almost the same end Solid carbon dioxide may be used.

## SENILE KERATOSIS

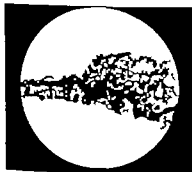
**Symptoms.**—These circumscribed horny lesions are flat, dry harsh and brownish occurring by predilection on parts exposed to sunlight Collectively they comprise a series of superficial epidermal neoplasms composed of keratinizing epithelium identical with the lesions of xeroderma pigmentosum and those provoked by carcinogenic agents such as tar dibenzanthracene and radiation It is common usage to apply the name precancerosis to individual lesions which are thought to be benign in their potentialities as the large majority of them collectively indeed prove to be However all intergradations exist between keratoses which peter out and drop off, keratoses which reach a certain stage of development and grow no further keratoses which slowly progress until they infiltrate the dermis and continue to grow as obvious carcinomas, and keratoses which progress speedily from the start into swiftly growing squamous carcinomas Therefore and in view of the fact that no sound prediction can be made about any given lesion at the moment of one's examination of it we group the lot as epidermal neoplasms (ADS 46 1 1942) *Their benignancy or malignancy is intimately associated* with the rate of growth and the cohesiveness of the neoplastic cells (Sutton ADS 37 737 1938) We define degree of malignancy as time rate



Fig. 645.—Senile keratoses.



Fig. 646.—Senile keratoses.





Figs. 647 and 648.—Keratoses from hair. Lesion is [illegible] because circumscribed portion of epidermis consisted of abnormal cells, sharply demarcated from normal ones, exceeding normal ones in rate of growth, and abnormally coherent as evidenced by coherence of corneum they have produced.



Fig. 649.—Early squamous carcinoma clinically a warty keratosis. Discoid and sharply circumscribed replacement of epidermis and warping of expanding disk of neoplastic epithelium, which coheres in keratinization so as to produce a horn.



Fig. 570.—Early squamous carcinoma. Topography revealed by section traversing from normal on one side to normal on the other. A "keratosis" 4 mm. in diameter from helix. Neoplastic cells have at 1 completely replaced normal ones so that epidermis here is composed of cancer cells only. The abnormal keratinization accounts for scaliness. Zone 2 would be called erythroplakia if it occurred on mucous membrane. From 2 neoplastic epithelium 3 has proliferated and expanded three-dimensionally at the dermo-epidermal junction, so as to lie adjacent to superficial portions of follicles and glands 7. Neoplastic epithelium 8 folds as the layer of it expands. Sections of folds 3 are two-layered. Terminations 5 of sheet of neoplastic epithelium are definite. Shearing stress of growth at dermoepidermal junction produces apparent space 4, an artifact. Erroneously interpreted as a separation of basal layer, this 4 is in fact replacement of basal layer by cancerous epithelium, which is spreading centrifugally. See Fig. 571. See ADS 46: 1, 1942.




Fig. 571.—Read legend of Fig. 570. See ADS 37: 737, 1938.



Fig. 572.—Early carcinoma. Compare Fig. 570 carefully; this is farther advanced. Compare Fig. 571.

of doing harm, a definition which makes the observer's knowledge of malignancy dependent on observations of a particular lesion over a period of time.

Senile keratoses are flat or verrucose. Sometimes they surmount a more or less narrow peduncle so as to resemble filiform warts. The scale produced by the proliferation of the epithelium of which they are composed, is harsh and horny. It may be of greater or less degrees of cohesiveness so that in one lesion there heaps up a horn of translucent yellowish appearance tightly applied at its base and in another there scale off flakes in thin laminae. If one picks off the scale, one tears through the thin epidermis so that bleeding occurs. While the majority of individual lesions never progress into actively invasive carcinomas, some 20 to 25 per cent of them do according to the guess of Montgomery (ADS 39: 387 1939). Fast growing keratoses are set on an inflamed base and are narrowly surrounded by a zone of hyperemia. These are early carcinomas.

**Etiology.**—Age is an important factor. An important element is a peculiar quality of the skin, a quality which is usually inherited and characterized by harshness, dryness and a tendency to freckle. Persons with such skins generally have reddish hair whether light or dark in color and are sensitive to sunlight. Such a skin with keratoses, is sometimes called "sailors skin" or "farmers skin". There are reasons for believing that a keratosis is a colony of cells which are the progeny of a somatic mutant. The initial change is intracellular, inherited by daughter cells, and irreversible (Sutton ADS 37 737 1938).

**Pathology.**—An early neoplastic keratosis is a small, roughly circular anomaly of the epidermis, which in that area is slightly browner or pinker than normal and may or may not possess a palpable harsh scale. In this stage, the microscope reveals epidermal changes which have been variously interpreted as "unrest" or carcinoma in situ or as separation of the basal layer from the remainder of the epidermis. Beneath the abnormal epithelium there is a more or less intense infiltration of leucocytes. The scale is parakeratotic in the places in which it is derived from the "restless" epithelium. This atypical epithelium spreads, undergrows and permeates normal epidermis.

In some keratoses which scale off readily so called separation of the basal layer is likely to be found. We believe that this is no down-budding but that neoplastic epithelium is here undergrowing, spreading and warping beneath the normal layer. In other keratoses which scale off readily the microscope shows atypical epithelial cells spreading through the epidermal layer in small groups or even singly evincing no tendency to cohere with one another. They cause by their proliferation a thickening of the epidermis, a filling and bulging of its papillae, an appearance of "unrest" and a form of keratinization which is irregular and in part parakeratotic. In this kind of keratosis the cells may be hydropic so that the lesion cannot be differentiated from Paget's disease or Bowen's disease. It is abnormal keratinization by cells we consider neoplastic which in the aggregate is by some observers called "dyskeratosis". While some keratoses scale off readily and are composed of cells which have no great tendency to adhere to one another or to form thick layers or large aggregates, many keratoses are made up of epithelium which persistently remains multilayered. This coherent epithelium thickens, forms comparatively dense horn, proliferates and expands in area, with the result that it buckles and warps and produces lesions which are clinically warty or hornlike. The continued cellular proliferation of a precancerous keratosis, by warping and buckling of its layers, eventually leads to entry into the dermis. There the cells proliferate freely without wastage by keratinization (Montgomery AmJCan 20 1934) and produce the intracutaneous lesion of slow or speedy rates of growth which are carcinomas of different degrees of malignancy. Keratoses are intraepidermal carcinomas.



Fig. 873.—Early squamou carcinoma from nose. Wartlike in ppearance this is histologically ob ious carcinoma. W rts do not degenerat into carcinomas little, wartlik carcinomas grow into big carcinomas.



Fig. 874.—Early squamou ca inoma. A pink sh papule with central horny spicul from the f ce. Complete replacement of centr l zone of rlying epidermis ha taken place formi g horny pik. Cancer cells freely in d dermis, ker tinizing individually as w ll f small pearl.



Fig. 875.



Fig. 876.

Fig. 8 .—Eryth pl k

Fig. 876.—Keratos and n ileop indic ting relationship bet them. All ar blastomas each isind kin l in beha ior and clinical significance.

**Histogenesis of Squamous Carcinoma.**—While superficially located growth of neoplastic cells is productive of keratoid growth in the dermis results in carcinoma. Early squamous carcinomas of the skin are minute warty lesions, or minute dome-shaped papules with a central horny spike. The central cornification is characteristic of the lesions for it inevitably result from their manner of histogenesis. They begin in one or few cells of the epidermis and these cells proliferate so as to supplant the whole thickness of epidermis at that site. That portion of the corneum which is derived from the altered cells is different from normal corneum. Swiftly growing the altered cell soon invade the dermis, and their growth there may be in coherent masses the central cells of which cornify and form horny pearls; or their growth may be in incoherent isolated cells narrow strands or small groups. Degeneration and keratinization of cells lacking coherence lead to the appearance of highly anaplastic growth, signifying a high degree of malignancy. Pearl formation is well developed in lesion composed of coherent cells. Mechanical considerations make it evident that inability to metastasize and so malignancy is greater in lesions with cells which do not stick together (Sutton ADS 37 737 1938 46: 1 1942 Cowan CaRes 4 623, 1944; Se 103 34 1947)

**Leukoplakia.**—Mucosal surfaces are normally uniformly covered with epithelium translucent enough to permit the red color of underlying capillaries to show through evenly. When a zone of epidermis is neoplastic and cohesive the epidermal covering at that place is thick, and it obscures in a sharply marginated region the blood color beneath. Neoplastic leukoplakia is a keratosis on a mucous membrane.

**Erythroplakia.**—Some keratoses spread centrifugally in a considerable area before neoplastic cells, previously lost by exfoliation eventually find within the dermis a fertile medium where they speedily produce obvious carcinoma with infiltration, invasion ulceration and metastasis. When this process occurs on a mucous membrane the lesion is called erythroplakia. It is clinically a velvety reddish plaque with thin and fragile epidermis, bleeding readily when subjected to friction. See Sulzberger and Satenstein (ADS 28 798 1933) Irgang and Alexander (ib 34 247 1936). Analogously on the skin, dry psoriasiform lesions are sometimes seen (Savatard BJD 5 87 1940). Treatment requires adequate surgical not radiologic destruction.

**Treatment.**—Men whose faces are affected should shave carefully to avoid nicking the lesions, for to do so is likely to plant their atypical epithelium within the dermis, where it can grow into carcinoma. The patient should diminish his exposure to sunshine. A thin coating of zinc oxide ointment may be helpful to persons occupationally unsheltered. Advanced keratoid lesions resist ointment therapy, which merely removes corneum while underlying cells continue to proliferate. These must be destroyed. One thorough freezing with solid carbon dioxide will do it. We find the microcautery efficient. Having obtained local anesthesia with procaine the point at high heat is wiped quickly over the lesion an application sufficient to blister off all epithelium. The wound heals in from 7 to 10 days, often without a scar. If the operation is too shallow recurrence as intracutaneous carcinoma may be expected. Admirable results can be obtained by the use of x rays or radium using a dose which peels. In growths which are already intracutaneous and progressive treatment is that of carcinoma. Vitamin A 100 000 units per day by mouth for several months, sometimes is notably salutary (Dublin and Hazen ADS 57 178 1948)

## CUTANEOUS HORN

Elongated epidermal growth composed of corneous material and originating from a circumscribed zone of epidermis ... occasionally seen. They do not overlie ... frame as do horn of cattle. Keratotic neoplastic growths, which are ...

cerous lesions of low malignancy often assume the clinical form of a horn. The lesions range considerably in outline and may be conic or cylindric straight, twisted, or angular The growths may persist or spontaneously drop off and recur Often they develop into manifest carcinoma. Excision is the therapeutic method of choice. The horny mass can be torn off and the base eradicated by thermocautery or roentgen therapy Astonishing cases are occasionally seen (Charache AmJSurg [illegible]: [illegible] 1935; Brown: NEngJM 232: 41 1945 Walker BJD 59 54 1947)

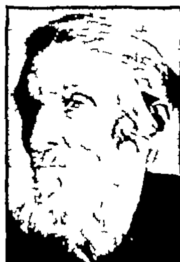


Fig 377



Fig 378

Fig 377 —Cutaneous horn a low-grade squamous carcinoma with coherent cell
Fig 378 —Cutaneous horn, histologic structure.

## CARCINOMA OF THE SKIN

Carcinomas are made up of epithelial parenchyma and connective tissue stroma. The stroma may consist largely of newly formed tissue, as in pedunculated and expansile growths, or it may be derived from both old and new fibrous tissue the former being supplied by the involved organ and the latter by proliferation of preexisting connective tissue The active agent is the living neoplastic epithelial cell All manifestations are secondary to it and dependent on it. In general the more rapidly a carcinoma grows, the less its cells resemble normal ones and the more intense the inflammatory reaction it induces.

**Classification.**—Cutaneous carcinomas are classified according to the types of cells which their cells resemble See Pinkus (JMichSMS 37 533 1938) Beerman (AmJMSc 211 480 1946)

Squamous Carcinomas are epithelial blastomas with cells like those of the rete they are characterized by the occurrence of keratinization of decadent cells so as to form pearls within the larger aggregates, and by their capacity for metastasizing.

Basal cell Carcinomas are comparatively benign growths, which do not metastasize and are composed of small, deeply staining epithelial cells of various sizes and shapes.

Transitional-cell (Baso squamous) Carcinomas are epidermal tumors composed of an admixture of basal and squamous-cell architecture which may or may not be homogeneous.

SPINDLE-CELL CARCINOMAS, the rare type established by Martin and Stewart (AmJCa 41: 273, 1935) may be considered one form of anaplastic squamous carcinoma. Two cases occurring, as usual, in radiation dermatitis, were noted by Sims and Kirsch (ADS 57: 63, 1948)

ANAPLASTIC CARCINOMAS, composed of loosely aggregated cells which undergo individual rather than group keratinization, are members of the squamous-cell type, comparatively highly malignant.

**Multiple Tumors** occurring simultaneously result from multiple pilosebaceous anlagen, yielding basal cell tumors, or grow from senile keratoses, yielding mainly squamous cell tumors. See Phillips (SMJ 35: 683, 1942); Tullis (JLCM 27: 688, 1942); Nisbet (ADS 47: 37, 1943); Cooper (SCNAm 24: 1022, 1944)

**Occupational Cancer** occurs in susceptive skins much exposed to sunlight (Phillips: TexasSJM 36: 613, 1941) in workers with tar and pitch, in workers exposed to absorption of arsenic, and in mule spinners (Brockbank: BMJ 1 622, 1941)

**Early Squamous Carcinoma** is described on pp. 614 619

**Cancers of the Mucous Membrane**, which are of malignant character and usually rapid development because of the loose and well nourished tissue into which they are free to grow spring from the leukoplakic or erythroplakic squamous cell covering of mucosal surfaces of the lips, tongue, gums, and elsewhere. They either ulcerate or vegetate, invasion signifying high malignancy and heaping up portending evil that is less urgent. Early mucosal carcinoma is discussed on pp. 617 623 and 701.

**Carcinomas of Cutaneous Accessory Structures** usually are of basal cell type. (See pilosebaceous adenoma p. 604; also p. 627 )

**Malignancy** a descriptive term, refers to capacity for and speed of doing harm. The word may be restricted in meaning to signify a capacity for metastasis in contrast with a capacity merely for local growth It is generally loosely used. Malignancy should be a strictly clinical word the microscopist can only say that he thinks the tissue came from a lesion which will behave as a malignant tumor (Sutton ADS 46 1 1942) The rate of ulceration is related to malignancy being roughly directly proportional except in highly malignant lesions, where invasion is rapid and only small central ulceration appears until late (Wilson ADS 41 667 1940 Broders grading) The size of the lesion when treatment starts is inversely related to curability Warren and Hoerr (SGO 69 726, 1939) reported 7 per cent mortality from lesions 1 cm in diameter or smaller 62 per cent mortality in lesions 5 cm in diameter or larger

**Metastasis** is the transplantation into a new site, distant from the primary field of growth, of neoplastic cells capable of continued proliferation. Lymph nodes are reached perhaps by insinuation of a narrow strand of growth, perhaps by ameboid movement of the cancer cells themselves, but most likely simply by currents of the lymph and tissue juices, which depend on normal drainage and muscle movements. The lungs, liver and other structures are generally reached via the blood stream See metastatic carcinoma p. 660. Cancer cells breed true Those in the metastasis are exactly like some of those living in the primary lesion.

**Recurrence** of a tumor which has been excised or otherwise destroyed is interpreted indubitably to imply that not all cancer cells had been reached in the initial therapeutic effort. A frequent cause of recurrence after treatment of cancer of the skin is the failure to recognize the fact that leucoplakia or keratosis surrounding an ulcerative carcinoma is part of it a part superficially located and not as yet intradermal, but composed of the same breed of neoplastic cells.

**Mode of Onset.**—A lesion which has arisen from a pimple, which the patient mistook for a blackhead and squeezed, is likely to be basal-cell cancer A lesion which developed from a scaly place which scaled off repeatedly and finally began to bleed, usually proves to be squamous, particularly if it arose on an exposed area of a sun-sensitive skin.

sharply marginated, irregularly outlined area of raw beef appearance, described as erythroplakia, a form of early epidermal neoplasia. It tends to spread laterally and sooner or later ulcerates, so that its carcinomatous nature becomes evident. In treating it, the entirety of the neoplastic surface must be destroyed at once, not piecemeal, for if only a part is cauterized the defect epithelizes in healing by proliferation of adjacent carcinomatous epithelium, and the result is worse than unsatisfactory. When carcinoma develops in leucoplakia, the leucoplakia which surrounds the ulcer



Fig. 893.



Fig. 894.



Fig. 895.

Fig. 893.—Advanced carcinoma, rodent ulcer. (Dr Fred H ...per.)
Fig. 894.—Advanced carcinoma of lip.
Fig. 895.—Advanced carcinoma of buccal mucosa with destruction of cheek.



Fig. 896.



Fig. 897.

Fig. 896.—Advanced carcinoma of lip, probably still curable.
Fig. 897.—Ulceration through skin and vegetation of metastasis in lymph nodes.

is composed of cancerous tissue. Sharply marginated, like the scaly keratosis found about many squamous carcinomas of the skin, such leucoplakia is the epidermal extension of the carcinoma. The leucoplakic margin, being part of the tumor, must be destroyed. The intraepidermal spread of carcinoma about the main tumor mass is easily discerned on careful examination and constitutes the reason for traditional wide excision or the wide application of radiation therapy. In mucosal carcinoma lymph node involvement speedily occurs, and pain is an early and persistent feature.

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**Location** is to some extent correlated with the type of tumors one may expect to find (Sutton JMoSMA 39 203 1942 Schrek and Gates APath 31 411 422, 434 1941)

EAR.—The large majority of cases are squamous. Surgery is advised because a curative dose of radiation will also destroy cartilage (Driver and Cole AmJR 48 66 194 )

EXTREMITIES.—The large majority of the lesions occur on the dorsum of the hands, and these are generally squamous in type (Braddon MJAustral 1 368 1944) Actinic and x ray dermatiti are common causes. Most of the lesions on covered parts of the extremities are basal-cell tumors. Half f all malignant melanomas originate on the soles. Correlating the size and prognosis in 2 cases of squamous carcinoma of the dorsum of the hand Clark and Johnson (JKansMS 49 100 1948) reported mortality over 80 per cent if the primary were 5 cm. in diameter or larger and at 3 cm. the lesion was highly dangerous.

EYELIDS are the seat of several kinds of tumors in addition t inflammatory new growths chalazion, adenoma or carcinoma of the Meibomian glands papilloma nevus, sebaceous cyst and riferous cyst angioma, and fibroma. Basal cell carcinomas are commonest. Surgical treatment is usually preferred (Hollander and Krugh AmJOphth 44 1944) although with proper protection f the e e radiation can be accomplished with excellent effect (Driver and Cole AmJR 41: 616 1939; Hunt ib. 57 160 1947) See Strond and Stewart (TexasSJM 36 426 1940)



Fig. 479.



Fig. 480.

Fig 479 —Squamous carcinoma a small, dome-shaped, warty nodule, with the usual central horn) spik

Fig 480 —Squamous carcinoma the central pik has increased t a wide crust.

FACE —About half the cases re squamous and half basal. A majority f those on the pper lip nose and forehead re basocellular

LIPS.—Lesion riginating on the ermil on portion f the lower lip are squamous. The starting place the l ne of closure where sal va is desiccated and t bacco tar in smokers, is concentrated this line is not the mucocutaneous junction. The lower lip support the vast majority of lip carcinomas because of its exposure to sunlight and males are subject t this disease 50 to 100 times as frequently as females. Lesions originating in the skin nea the mucocut neou junction re usually f basal cell nature.

MOUTH AND TONGUE.—Epithelial tumors are al ay squamou with the occasional exception of tumors arising in sal ry gla ds (see mixed tumors, p. 644) New plastic lesions seen in the mouth include neurofibroma, angioma, cyst, rhabdom oma, adamantinoma, et

PENIS.—Lesion here are squamou They sometimes begin in the form of erythroplakia. Unabbreviated foreskins pred pose (Plaut and Keh Speyer) Ne 103: 391 1947) Treatment is surgical (Carson JUrol 41 30 1940)

SCALP —Cysts and nevi are commonest and squamous carcinoma may evolve from a cyst. Seborrheic keratoses, melanoma, lipoma, basal cell carcinoma, and metastatic lesions in the skin are also seen (Love: MPKClin 32: 196, 1944)

SCROTUM.—Here the lesions are squamous, and are usually related t occupation. Henry (AmJCa 31 [illegible] 1937) found 1 45 fatal cases in England and Wales in the period 1911 to 1935, and all but 13 were carcinomas. Of 103 cancers in chimney sweeps only 44 were not scrotal. All cancer deaths in chimney sweeps which occurred before the age of 45 years were due to scrotal carcinomas

VULVA.—Squamous carcinoma is the usual nature of the rare carcinomas here Syringoma (q v) is more common. Other tumors in this location include fibroma, lipoma, hemangioma, endometrioma, cyst and melanoma (Wilson ASurg 43: 101 1941 Taussig: AmJOG 40: 764, 1940 Folsome J 114: 1499 1940)

## SQUAMOUS CARCINOMA

**Symptoms.**—An epidermoid or prickle cell carcinoma is a malignant growth originating in epithelium and characterized by cells resembling those of the squamous layers of the epidermis in that they undergo keratinization when they degenerate. Their histogenesis is described on page 619 Pain is not a prominent feature until late in the disease. The earliest perceptible lesion in squamous cancer of the skin is a roughened, warty keratotic patch or senile keratosis, or a small reddish or yellowish circumscribed nodule from the center of which projects a horny spike. In a few weeks or months some portion of the gradually enlarging growth ulcerates. The superficial ulcer is at first partially hidden by scales and crusts. The base is always sharply defined and more or less indurated, reddish because of dilation of near-by capillaries. The lesion increases in size by peripheral extension and increment of central ulceration The edges of an advanced tumor are hard, everted, and generally undermined. As the growth extends, connective tissue cartilage periosteum, and bone are attacked. Lymph node involvement follows sooner or later the tumors evincing great individual differences in their ability to metastasize and their rapidly in doing so. The development of secondary tumors in internal organs is an occasional sequel. Most patients are middle-aged or elderly individuals. The sites of predilection are the face particularly the lower lip, ears, and dorsa of the hands. Vegetating carcinoma may be papillomatous from the beginning or it may develop from an ulcerative lesion, becoming cauliflower like with a verrucose surface covered with tenacious, foul smelling, yellowish, purulent exudate Comparatively benign pseudo-actinomycotic lesions are occasionally seen (Charache ADS 43 609 1941)

**Carcinoma of the Mucous Membrane,** malignant squamous carcinomas, affect mucosae of the tongue, buccal, oral, and nasal cavities, and vagina rectum and balanopreputial sac. On the tongue and buccal mucous membrane the disease may begin with small or widespread superficial, reddish alteration, or with a minute fissure having infiltrated base. A fever blister of the lip which failed to heal, is a common story Neoplastic leucoplakia (p 701) bears the same relation to mucosal carcinoma as senile keratosis to cutaneous carcinoma P rsons with oral carcinoma are as regularly of sun-sensitive complexion as persons with squamous carcinoma of the exposed skin

Leucoplakia is white because of the thickness of epithelium of which the lesion is composed. If instead of heaping up and clouding the visibility of underlying capillaries, the abnormal epithelium exfoliates readily and forms only a thin covering for the mucosa, the clinical manifestation is a



Figs. 331, 332, 333 and 334.—Squamous carcinomas of the hand.



Fig. 335. Fig. 336. Fig. 337

Fig. 335.—Ulcerative squamous carcinoma.
Figs. 336 and 337.—Wartlike or hornlike squamous carcinomas.



Fig. 338.



Fig. 339.

Fig. 338.—Squamous carcinoma of woman upper lip.
Fig. 339.—Advanced carcinoma of lower lid. (Dr. W. Herbert Brown.)



Fig. 330.—Keratoses and carcinoma of xerotic skin of a blond farmer



Fig. 331.—Keratoses and deeply invasive carcinoma of temple.



Fig. 332.—Squamous carcinoma on scar of burn.

sharply marginated, irregularly outlined area of raw beef appearance described as erythroplakia, a form of early epidermal neoplasia. It tends to spread laterally and sooner or later ulcerates, so that its carcinomatous nature becomes evident. In treating it, the entirety of the neoplastic surface must be destroyed at once, not piecemeal, for if only a part is cauterized, the defect epithelizes in healing by proliferation of adjacent carcinomatous epithelium, and the result is worse than unsatisfactory. When carcinoma develops in leucoplakia, the leucoplakia which surrounds the ulcer



Fig. 893.



Fig. 894.



Fig. 895.

Fig. 893.—Advanced carcinoma, rodent ulcer. (Dr. Fred Harper.)
Fig. 894.—Advanced carcinoma of lip.
Fig. 895.—Advanced carcinoma of buccal mucosa, with destruction of cheek.



Fig. 896.



Fig. 897.

Fig. 896.—Advanced carcinoma of lip, probably still curable.
Fig. 897.—Ulceration through skin and excavation of metastasis in lymph nodes.

is composed of cancerous tissue. Sharply marginated, like the scaly keratosis found about many squamous carcinomas of the skin, such leucoplakia is the epidermal extension of the carcinoma. The leucoplakic margin, being part of the tumor, must be destroyed. The intraepidermal spread of carcinoma about the main tumor mass is easily discerned on careful examination, and constitutes the reason for traditional wide excision or the wide application of radiation therapy. In mucosal carcinoma lymph node involvement speedily occurs, and pain is an early and persistent feature.

**Etiology.**—The essential cause of carcinoma is unknown. Heredity is probably a predisposing factor. The role of chronic irritation, once considered paramount, is open to question, and the part played by trauma is dubious. Spontaneous, or induced by various agencies, the primary change seems to be one which affects the reproductive mechanism of the cell. Once altered, the cell is permanently different and its progeny are similarly different from normal in appearance and behavior. The ability to grow where normal cells do not, invasiveness, and the inability to produce normally organized tissue structures are characteristics of neoplastic cells.

The disease is usually one of adult life. Men are attacked 3 times more frequently than women (Broders, J 74: 656, 1920). Carcinoma of the lower lip is almost exclusively a disease of males. The white race is more susceptible than the Negro.

Mechanical, chemical, thermic and actinic influences are significant. Pipe smokers' cancer and chimney sweeps' cancer are recognized; workers in tar and paraffin, and farmers and sailors exposed to sun and wind, are frequent victims of the disease. Mule spinners' cancer develops on the scrotums of cotton spinners in Great Britain, due to oils used in the lubrication of machinery. Cook and Kennaway were able to obtain chemically pure, carcinogenic hydrocarbons, and their work has greatly stimulated investigations in this fruitful direction. The carcinogenic action having been exerted and cancer initiated, no further part is played by the chemical agent. See Cook et al. (AmJCa 29: 219, 1937; 33: 50, 1938; 39: 381, 428, 521, 1940). Occupational cancer due to pitch and tar was discussed and well illustrated by Ross (BMJ 2: 369, 1948). Smegma is of interest as a carcinogen, for circumcized males do not develop cancer of the penis. Its carcinogenicity is shared by other fatty substances of biologic origin (Edit., BMJ 1: 987, 1948).

The lesions occasionally develop at the site of old injuries, especially in scars following burns, roentgen dermatitis, lupus vulgaris, lupus erythematosus, and gummatous ulceration. Ulcers associated with osteomyelitis may be the starting point; the neoplastic epithelium invades the marrow spaces and necessitates amputation. Tobacco contributes to the development of cancer of the lip and mouth (Friedell and Rosenthal, J 116: 2130, 1941). Trauma as an initiating factor is discussed by Leighton and Schmidtke (JMoSMA 37: 267, 1940) and Warren (AnnSurg 117: 585, 1943). See Plummer-Vinson syndrome (p. 447); also Kraurosis (p. 564).

PRECANCEROSIS.—There are several dermatologic lesions in which or on the basis of which carcinoma develops by predisposition. While we have seriously objected to the term "precancerous," it is a word in common use. MacKee and Cipollaro (Cutaneous Cancer and Precancer, Lancaster Press, 193 ) listed as comprising precancerous dermatoses:

| | |
|---|---|
| Cicatrix | Lupus erythematosus |
| Cutaneous horn | Lupus vulgaris |
| Erythroplakia | Nevi |
| Farmers' or sailors' skin | Radiodermatitis |
| Keratoses | Sebaceous cyst |
| Arsenical | Syphilis (syphilitic leucoplakia, glossitis, syphilitic scars) |
| Seborrheic | Ulcers (long standing) |
| Senile | von Recklinghausen's disease |
| Occupational (tar, pitch, oil) | Xeroderma pigmentosum |
| Kraurosis | |
| Leucoplakia | |

Paget's disease and Bowen's are omitted because many authorities agree that they are cancer from the beginning.

*When cancer begins, it does so at a point where arises [illegible] from which spreads the same sort of [illegible] neoplastic lesion which appears as [illegible]*

*carcinoma may come into existence.* Keratoses following x ray burns or applications of carcinogenic agents are not different from other keratoses.

ARSENICAL CARCINOMA.—Arsenic as a cause of carcinoma was recognized by Hutchinson in cases of psoriasis treated with arsenic with resultant neoplasia. About one-third of arsenical cancers are basal cell in structure, although most are squamous; and metastasis may occur despite the apparently low grade of the tumor Inorganic arsenic is far more dangerous than organic. Arsenical keratoses, typically involving the volar surfaces, may become cancerous or may undergo involution particularly if the ingestion of the drug is stopped. See Montgomery and Waisman (JInvD 4: 365, 1941) Multiple, superficial, basal-cell epitheliomas of the trunk are usually arsenical in origin, the arsenic having been absorbed perhaps 20 years prior to the appearance of cancer

LIGHT is a recognized influence in the causation of cancer of the skin (see senile keratosis and xeroderma pigmentosum) Light seems to act on nuclei of cells in the same manner as other electromagnetic energy including x rays. See Blum (JNatlCaInst 1: 397 1940 3: 91, 1942) Taussig and Williams (APath 30: 721, 1940)

EXPERIMENTAL CARCINOGENESIS.—Yamagiwa and Ichikawa (JCaRes 3: 1, 1917) showed that the repeated application of tar t a rabbit s ear will provoke warty growths, some of which become malignant. Many investigators have pressed the advantage of the valuable knowledge that cancer can be provoked experimentally and researches with pure chemical substances, particularly the benzopyrene derivatives, are continually fruitful. The carcinogenic properties of cysticercus infestation, scarlet R viruses, spiroptera infection, occupational materials and chemicals including dyes, ta soot, oils and the like, are merely mentioned here. See Dunning et al. (AmJCa 28 681 1936) Milder and Morton (AmJPath 15: 299 1939); Pullinger (JPathBact 50 463 1940) Rous and Kidd (JExpM 73 365 391 1941); Berenblum (CaRes 1: 807 1941); Cowdry (JInvD 6: 15, 1945) Monographic is Furth (AnnRevPhysiol 6: 23, 1944) The carcinoma cell constitutes a new cell type in a given host with a varying degree f deviation from normal and limitation of freedom from forces controlling normal growth. Re mutation theory see Sutton (ADS 37: 737 1938; 46: 1, 1943)

VIRUSES are known to cause carcinoma. The rabbit papilloma, resembling the human condyloma acuminatum, frequently becomes malignant (Shope: JExpM 58: 607 1933) See Rous (AmJCa 28 _33, 1936) and Edit. (J 103: 394, 1937)

**Pathology**—In squamous carcinomas, long, fingerlike epithelial projections extend into the connective tissue and round pearly masses, made up of cornified epidermal cells, are formed both in the subjacent structures and in metastases in the lymph nodes. The growth spreads out like the roots of a tree, and a single cross section may show groups of isolated cells and pearly masses which, followed three-dimensionally prove to be connected with the rest of the growth. The pearls are groups of cells arranged concentrically and presenting changes progressively from the periphery toward the center corresponding to the changes in the normal epidermis from the deep layers to the surface. Keratinization is irregular and parakeratotic

To distinguish histologically between pseudoepitheliomatous hyperplasia at the edge of an ulcer and carcinoma developing at the edge may be not only difficult but actually impossible (Winer ADS 42 856, 1940) Infiltration must extend into the level of the sweat glands if one is to be comparatively sure. Clinical behavior not morphologic histology is the final criterion

GRADING.—Broders (AmJR 4 17 90 19*7) separated squamous carcinomas on histologic examination into four grades dependent upon the relative proportions of differentiated and undifferentiated cells, Grade I being least malignant and Grade IV most malignant He found good correlation between his pathologic grade and the actual result in the case so that grading seemed to be of prognostic importance. While the service so rendered may be of aid to surgeons unfamiliar with microscopic architecture we believe that what Broders called differentiation is i fact degeneration and that the outcome in a given case depends on the removal or incapacitation of all cancer cells whatever grade they may be assigned to; and that such removal

is easy in small lesions and difficult in advanced ones without regard to the grade; and that, in carcinomas in whi h the cells proliferate with little tendency to adhere to each other the removal of all of them is on that account rendered difficult, for they diffuse through the tissues and metastasize readily as compared with tumors in which cells tend to cohere and to form well-developed horny pearls; and finally that the business of grading is permeated with subjectivity while it loses sight of the fact that *a tumor is as malignant as its most malignant part* a part which may elude the examiner

**Diagnosis.**—Biopsy is the final criterion, but the clinical character of the lesion generally suffices for recognition. The history and the age of the



Fig. 198.—Gross section of squamous carcinoma, 2 cm. in diameter widely excised so as to amputate all tumor tissue successfully. Knowledge of whole-tumor architecture is essential to intelligent treatment. (Stout Human Cancer Lea & Febiger 1932.)



Fig. 199.



Fig. 200.

Fig. 199.—Squamous carcinoma. Infiltration by narrow strands, and horny degeneration of all but peripheral cells of every aggregate more than 3 or 4 cells thick.

Fig. 200.—Squamous carcinoma. Normal epidermis is seen t lower right, with sharp change in cell type at edge of cancerous proliferation. Cancer cells fill the dermis and undermine the edge of normal epidermis.

patient are also suggestive. The growths are usually single, and of slow development. They tend to ulcerate early and are frequently covered by a thick crust. In mucosal carcinomas, the bases of the lesions are more or less indurated and generally are surrounded by leucoplakia. Lymph node involvement occurs late, and is usually regional and localized. It is an error to await therapeutic response in differentiating syphilis and carcinoma of the tongue. The dangers of biopsy are inconsequential. Small lesions should be removed in toto, not nibbled at with equivocating diagnostic efforts. Biopsies are seldom necessary for diagnostic doubt can exist only when the observer is amateur or the lesion is small, in which case it should be excised and examined microscopically as a whole.

**Prognosis** depends on duration, extent, location of the lesion possibility of its total mechanical removal, presence or absence of metastases, and radiosensitivity of its cells. The outlook is especially grave if the growth is in the mouth The earlier treatment is instituted, the greater the chance of cure Previous treatment that has failed greatly lessens the patient's chance of ultimate recovery

If it is possible to surround and destroy the entire neoplasm or permanently to incapacitate every one of its cells by radiation, if this can be done without killing the patient and if it is done without contaminating the operative field with viable cells, even carcinoma with metastasis can be permanently cured. Small growths still localized lend themselves to cure if the patient is cooperative almost invariably In performing therapeutic destruction, which is the basis of all means of curing cancer one must sacrifice normal tissue beyond the margins of tumor growth without timidity regarding cosmetic results.

**Treatment.**—Curative treatment of squamous carcinoma of the skin consists in the removal or destruction of the cells by various means. This can be accomplished by excision, curettage cauterization with chemicals or by means of the actual cautery endothermy and the x rays or radium The sine qua non of intelligent therapeutic effort is knowledge of the exact extent to which one wishes to destroy and of the extent to which the agent acts, and it presupposes knowledge of the natural history of the tumor Gross and microscopic studies of whole tumor sections, and clinical experience are means for obtaining such knowledge. The ideal choice [of a particular form of treatment] can only be made if all forms of treatment are available and if the choice is independent of any vested interest in an x ray machine a quantity of radium or the possession of the requisite skill and courage to undertake major surgical operations (Cade Malignant Disease and Its Treatment With Radium Wood 1940) See Eller (Tumors of the Skin 1939 Lea & Febiger)

CAUTERY—*In our practice we depend more and more on the electrocautery* Properly used, we have found it to be the most valuable of all agents in combating cancer of the skin Many but far from all, dermatologists share this belief Under local infiltrative anesthesia the *excision is made through normal tissue surrounding the neoplasm* The wound is allowed to granulate under simple ointment dressings Fulguration and similar methods offer nothing particularly advantageous. Their action is not selective See p 61

SCALPEL.—Surgical excision with the ordinary blade has become increasingly acceptable in the removal of both the primary and regional involvement.

*chromosomes and genes. Coutard taught that a saturation method is most* efficient, treatment being not too protracted. Heavily filtered fractional doses are regarded as preferable by many authors. The dose is likely to be too small rather than too large. Martin and Wright (J 134: 861 1947) recommended for vegetative lesions 1 100 r at 85 kv with 0.5 mm. Al daily for 4 or 5 doses in lesions less than 2 cm. in diameter A dose of 300 r per day to a total of 3 600 or more is an alternative technic (Dowdy NYSJM 40 621 1940) or 400 r twice a week (Miescher RadiolClin 10 166, 1941) See symposium on treatment (ADS 53 563 ff, 1946) Trying doses at 200 kv ranging from 1,200 to 6 000 r., Hale and Holmes (Radiol 48 563 1947) cured about 94 per cent of previously untreated skin cancers by means of doses in the 2 500 to 2,800 r range, cured about 80 per cent with doses of 1,200 to 1,800 r and gained nothing by going above 2,800 r

Such procedure is curative, when it is, through the same necrotization as is achieved by surgery The difference lies in the fact that with the application of x ray everything in the path of the beam is killed willy nilly leaving a lattice skeleton of anuclear tissue into which inflammatory and *cicatrizing elements may grow while in the use of surgery someone's* judgment must be depended on as to what is destroyed and what is not It might happen that a tumor impossible to remove surgically should be destroyed by radical roentgenization. The procedure is as radical as surgery and this fact must be recognized by the physician and the patient. The latter usually imagines he is going to get off easier with the method of attack in which he is not cut on. When surgery is used, there is no radiodermatitis to combat later See pp 65 and 56

RADIUM is an efficient agent in attacking keratoses and superficial carcinomas. In deeply seated tumors, gamma ray methods should be employed and large exposures must be given. Cosmetic results are favorable, and the agent is simple and convenient. The necessity for adequate dosage must be stressed, and much disappointment will be avoided if the dosage is generous. Surface application is often inadequate. In lesions of the tongue in particular surface application of radium is never adequate. The use of needle implants has been well described by Cole and Driver (AmJR 33 682, 1935) A gamma ray dose of 6000 r is generally tumor lethal (Paterson and Parker BJRadiol 7 592, 1934) See p 60

*CANCER OF THE MOUTH —The difficult problems involved require judg*ment which must be derived from experience and wide reading Early treatment is essential Leucoplakia and erythroplakia must be recognized—the informed dentist is a help here—and they must be adequately treated by proper destruction chemical cauterants such as silver nitrate being generally harmful and deplorable in their effects. Richards (CanadMAJ 35: 593 1936) cured over 90 per cent of those seen early in advanced cases he was able to heal the primary site in about half the cases by the use of radiation One method of attack is to implant radium emanation (radon seeds) one millicurie of radium emanation to each cubic centimeter of tumor giving also deep roentgen therapy to the cervical region.

MANAGEMENT OF LYMPHATICS.—This question may be resolved into two parts what to do when the nodes are not palpable, and what to do when they are. In oral cancer Padgett (Surgical Diseases of the Mouth and Jaws, Saunders, 1936) preferred to remove the nodes before there appeared evidence of metastasis in them but if operation is refused, x ray treatment should be given. Wile and Hand (J 108 374, 1937) believed that node

treatment is unnecessary unless the nodes are palpable. Invasion of the mandible, in cancer of the lip, forebodes practically inevitable death. Of 258 cases without evidence of metastasis at first visit, only 8 developed it after eradication of the primary lesion (Hall AmJR 38: 116, 1937) We favor waiting for palpable involvement, then attack surgically

SURGERY WITH RADIATION.— It has been urged that, if postoperative radiation is given, it should be done exactly as if no operation had been performed. Postoperative irradiation is not indicated unless the surgeon fears his work has been incomplete His fear may be justified by considerations beyond his control. Preoperative radiation has fallen out of style.

CHEMOSURGICAL TREATMENT has been modernized by Mohs (ADS 56: 143 1947) who controls repeated caustic partial destruction by histologic examinations. We are convinced that a single surgical destruction can be done at least equally effectively from every standpoint and is much to be preferred. The horrors of escharotics, which can be curative, are described by Ackerman and Eberhard (JMoSMA 40 163, 1943)

CHECK-UP —The patient should be urged to return for observation at increasing intervals for a period of one, two or preferably five years.



Fig. 601



Fig. 602.

Fig. 601.—Palliative effect of radium treatment of advanced squamous carcinoma in an old man. Lesion as first seen

Fig. 602.—Lesion shown in Fig. 601 two months after 50 mg. radium point source had been set for 8 hours at the center of the defect. The carcinoma later caused the patient' death. A 32-hour dose would have been better adequate surgery better yet.

PALLIATION —Sympathetic, careful attention to incurable patients is appreciated. There is ample play for the art of the physician in managing the doomed. We are not successful with prevarication, and our patients regularly find out the truth and think the less of us when we try to hide it from them. A man with dependents for whom he must provide in a limited time is better served with facts than with deception. Morphine should not be withheld. Alcoholic injection of the Gasserian ganglion may control pain in incurable cancer of the mouth (Harris BMJ 2 831, 1938) X ray therapy for palliation is given in doses which do not sicken or cause violent reactions locally it may help a great deal. Cordotomy destroying sensory pathways may be undertaken (Grant J 116: 567 1941) Cobra venom in suitable doses gives effective relief of pain. Odor may be ameliorated by moist compresses of tartaric acid solution at a pH of 2.9 or

diiodohydroxyquinoline tablets (Karnaky J 122 780 1943) Skin metastases of certain carcinomas arising elsewhere may actually disappear under estrogenic hormone therapy See Daland (J 136 391 1948)

## BASAL-CELL CARCINOMA

**Symptoms.**—The comparatively benign variety of carcinoma of the skin develops from basophile cells resembling those of the basal layer of the epidermis or from accessory structures of the skin (see pilosebaceous adenomas) and does not metastasize. The rate of destruction is not so great in this as in the squamous variety but progressive ulceration can result. Men are attacked more commonly than women. Most cases occur in adults. They occur by predilection on the face but may develop anywhere on the skin, never on mucous membranes. The etiologic factor influencing location is not well defined as is the influence of sunlight in the etiology of squamous lesions. Nose, forehead, upper lip eyelids, and covered parts of the trunk and extremities are preferred.

Basal-cell carcinomas usually appear first as small, shiny whitish or reddish, translucent nodules. They may less commonly begin as scaly patches. Lesions may be single or multiple They give rise to no symptoms until after persisting for weeks or months they undergo ulceration. When this occurs it first involves the central part of the growth and the remainder slowly spreads peripherally Ulcerated areas may heal slowly leaving smooth or scaly atrophic cicatrices but progress continues at the periphery, and spontaneous healing occurs only in extremely rare instances. See Dunn and Smith (BJD 46 267 519 1934) Ayres (ADS 49 83 147 1944)

**Morphea like Basal-Cell Carcinoma.**—Intracutaneous, steadily progressive lateral extension is typical of this variety The advancing margin is band like and the scarred area is smooth, flattened, and ivory-colored, superficially resembling scleroderma. There is a characteristic raised, pearly, waxlike border Histologically these are of trichoepitheliomatous structure Cicatrization may be sufficiently potent to encompass tumor cell within dense fibrotic walls, so that some of them atrophy and perhaps disappear Self healing depends on this process, but it is only rarely productive of complete cure. In treating this type the usual error is to remove too little tissue. Radiotherapy is unsuitable, excision being essential

**Accessory Structure Basal-Cell Carcinomas** are thought to arise from hairs, sweat glands, or sebaceous glands in some instances. Malformed or anomalous accessory structures seem to act as initial lesions which, in assuming active growth after prolonged quiescence become carcinomas.

**Basal-Squamous-Cell (Intermediary Cell) Epithelioma.**—Tumors are frequently seen in which are combined the characters of basal cell and squamous types of structure. They can not be identified clinically but histologic study reveals the transitional character of basal cell architecture [illegible] and keratinizing cells They are capable of metastasizing and require treatment [illegible] for squamous cell carcinoma (Montgomery ADS 18 50 1928)

**Pigmented Basal-Cell Carcinoma.**— Melanotic rodent ulcer was the title given by Johnston (JCutD 23 63, 1905) This is a distinct type of basal cell tumor associated with pigment, easily confused with melanoma unless histologic study is made All basal cell tumors contain some pigment, but sufficient is present in only 6 to 10 per cent of them to justify the particular designation, pigmented. Differing from the pigmented acanthotic nevus (p 613) these comparatively benign lesions have the prognostic features of basal cell carcinoma, not of melanoma. The pigment cells scattered among the epithelial cases and also [illegible] quantities in the stroma, are distinct from the carcinoma cells and are dendritic [illegible] form, filled with melanin granules (Eller and Anderson ADS [illegible]7 1953

**Metastatic Basal Cell Carcinomas** have been observed in which regional lymph node involvement apparently has not resulted from mere extension. Such are extremely

rare (DeNavasquez: JPathBact 53: 437 1941 Auerbach: ADS 56: 173, 1947) Most of the few cases have originated in the scalp.

**Angiomatous (Hemorrhagic) Basal Cell Carcinomas** are characterized histologically by cavernous angiomatous spaces surrounding the basal cell proliferations. They grow and expand into the subcutaneous tissue are usually adherent to the epidermis, which may be elevated and discolored with a bluish hue, are encapsulated, and may feel cystic (Geschickter and Kensbey: AmJCa 23: 568, 1935, Lamb et al.: BMJ 36 132, 1943) Not radio sensitive they are readily cured by excision.





Fig. 909. Fig. 910.

Fig. 909.—Basal-cell carcinoma of the left temple.

Fig. 910.—Basal-cell carcinoma at the angl f the nose.

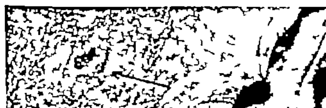
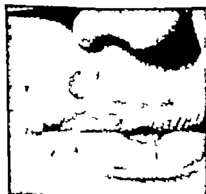


Fig 911.—Basal-cell carcinoma, early



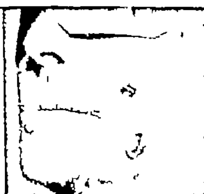


Fig 912. Fig. 913.

Fig. 912.—Basal-cell carcinoma of woman upper lip an intradermal, waxy discoid nodule, not ulcerated.

Fig 913.—Morphea-like basal-cell carcinoma of a woman face. During 10 years, progress from a central point ha led to this state, in which one sees scar that developed spontaneously and tw nodules of lcerating basal-cell carcinoma. Nodule on lower lip was neurilemmoma.

Lipoma Like Basal Cell Carcinoma is a rare sort in which the adenoid stroma forms a soft, bulging subcutaneous mass, elastic and lipomatoid on palpation, identified by histologic, not clinical, examination (Sutton ADS 43: 176 1943)

**Etiology**—The cause is unknown. Both basal and squamous lesions may be found in the same individual. Basal-cell carcinomas probably represent progressive growth of such anomalies as epithelioma adenoides cysticum. A history can generally be obtained of a preceding lesion a



Fig. 914.



Fig. 915

Fig. 914.—Basal-cell carcinoma. (Dr J P Ocequierra.)
Fig. 915.—Multiple basal-cell carcinomas.



Fig. 916.—Morphea like basal-cell carcinoma, showing threadlike pearly margin.

waxy pimple or blackhead-like lesion which the patient has picked. Sun exposure and x radiation predispose, as they do to squamous lesions. Histologic structure cannot safely be predicted before the microscope is used. See arsenical carcinoma. See Figs. 42 and 43

**Pathology**.—The development of the cancer masses can be studied best in small lesions. The process apparently begins in the basal layer of the epidermis or follicular epithelium. Tumor tissue can be differentiated readily from normal, to which it may lie adjacent. The configurations of cell-congeries seem governed by the resistance of the surrounding structures, the course and progress of the cancerous masses being dependent on the density of the tissues. Long sinuous strands of cancer cells may extend far into the dermis. They may coalesce. Epithelial lumps are often acorn-shaped, occasionally with a cystic, mucoid center which consists of disintegrated cancer cells. In slow-growing lesions, round cell infiltration in the vicinity is less than in fast-growing lesions. A thin layer of connective tissue frequently separates the tumor mass from the subpapillary stroma. The cells themselves are relatively basophilic, often spindle-shaped, and loosely or compactly grouped. An acinar or plexiform arrangement is common.

Foot (AmJP 23: 1 1947) confirming Mallory (J 55: 1513, 1910) and Haythorn (AmJCa 15: 1969 1931) recognized the analogy of basal-cell tumor development to pilar sebaceous, and sudoral units, with variation in differentiation. He classified adnexal carcinomas among three types (1) pilar proper primordial, or cylindric (2) sudoriparous, adenoid or hydradenomatous; and (3) basal cell. Any may be pigmented. A rich, nonmyelinated neural plexus is present in the tumors, which begin by loosening of elements of the rete near a hair or sweat gland, followed by the formation of small nodules in the dermis just outside the basal layer

Classification of tumors originating from the primary epithelial germ was undertaken also by Lever (ADS 57 679 700 1948) who explained the wide variety of histologic pictures by variations in degree and direction of differentiation prior to the onset of neoplasia. Lever discussed organic, organoid, suborganoid, and nonorganic hamartomatous tumor formation, each class being subject to sebaceous, apocrine, or hair differentiation. His organic hamartomas are organoid nevi, organoid hamartomas are adenomas, suborganoid hamartomas are benign epitheliomas, and nonorganic hamartomas are basal cell epitheliomas, which he would not call carcinomas because they do not metastasize.

**Diagnosis**.—The sharply defined and waxy character of the lesions, the absence of lymph node involvement, the comparatively slow growth rate, and the tendency to progress laterally help to distinguish them from the squamous variety The absence of apple-butter nodules should serve to exclude lupus vulgaris. The lesions may bear a superficial resemblance to serpiginous syphilids, but here, too, the shiny nodules of cancer tissue should serve for recognition. When the skin is stretched and suitably illuminated, the tumor tissue gives an appearance such as would an intracutaneous injection of paraffin. Histologic diagnosis is essential.

**Prognosis** in small basal-cell carcinomas is favorable. If neglected, however the tumors may give rise to great deformity particularly if the nose or eyelid is involved, and unchecked they progress to the death. Transition into squamous carcinoma may occur particularly if the lesions are inadequately treated with x rays then the prognosis is changed to that of malignancy with the possibility of metastasis.

**Treatment**.—Small growths may be curetted out, and acid nitrate of mercury then applied. X rays or radium may be employed with the doses and technic used in treating squamous carcinoma (p 631) Ber-



Fig. 917



Fig. 918.

Fig. 917.—Tiny basal-cell carcinoma. Whole-tumor section, showing topography mucoid cystic degeneration, and shrinkage of tumor masses due to fixation.

Fig. 918.—Tiny basal-cell carcinoma of nose, a waxy scaling pimple. Structure suggests fat gland origin.

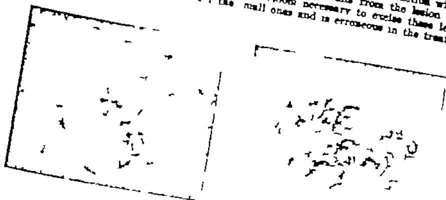


Fig. 919.—Basal cell [illegible] whole tumor section [illegible] low [illegible] showing structure of rolled [illegible] central crusted depression, and sharply delineated extent of growth. [illegible] structure and boundaries, as exemplified here underlies success in therapy.

In our opinion, the whole lesion may be excised by a destructive physical agent, such as the actual cautery. Cure consists in the total extinction or incapacitation of the neoplastic cells, preferably in a manner conducive to good cosmetic results. It is bad practice to use an agent without knowing accurately the destructive capabilities it possesses and their extent of action, and without accurate understanding of the gross and minute anatomy of the parts involved, and the natural history of the tumor.

## SUPERFICIAL CARCINOMAS

**Superficial Basal-Cell Epitheliomatosis** is characterized by the development of superficial, sharply circumscribed patches of scaling dermatosis simulating patches of psoriasis, generally on the trunk. The color is reddish, the outline irregularly oval, the scaling irregular, the margin definitely sharp if carefully examined, the duration considerable, and the symptoms slight or absent. The patches enlarge by irregularly centrifugal spread. Microscopic examination shows tumor tissue of basal-cell type closely applied to the undersurface of the epidermis is apparently isolated clumps. One, several, or many superficial basal-cell carcinomas may appear on one individual. Their fine, threadlike, rolled, pearly border is typical. Eventually there develop large cell-aggregates which vegetate or ulcerate and progress as ordinary basal cell carcinoma. Sections perpendicular to the skin have been interpreted as showing multicentric origin, but sections parallel with the surface indicate that the tumor tissue forms a network spreading radially at the dermoepidermal junction and apparently unifocal in origin (Madsen: Acta D-V 21: 514, 1940; 22: 24, 1941; abs YBD 1940, p. 310). Etiologically arsenic may play an important role (Anderson: ADS 26: 1033, 1933). Treatment is best accomplished by local or Pentothal anesthesia and superficial destruction with the actual cautery accomplishing a complete removal of epidermis from the lesion and a small margin of adjacent normal skin. It is seldom necessary to excise these lesions. Radiation therapy is suitable only for the small ones and is erroneous in the treatment of extensive plaques.



Figs. 9[illegible]0 and [illegible]1.—Bowen's disease.

**Bowen's Disease.**—Bowen (JCutDis 30: 241, 1912; 33: 787, 1915) described cases of atypical epithelial proliferation characterized by the development of firm, pinkish or reddish papules covered with a thickened horny layer, and tending to form rounded, nodular lesions. Mucosae are occasionally involved (Cipollaro: NYSJM 40: [illegible]4, 1940). Crusting is regularly present and when the surface débris is removed, the [illegible] beneath is red and oozing, granular, and sometimes papillomatous in appearance.

Histologically the lesions exhibit cancerous epithelium of a peculiar sort, limited, during the time when the lesion is still superficial, to the epidermal zone (Stout: NYSJ 39: 801, 1939; Johnson: BJD [illegible] 19[illegible], 194[illegible]). The cells are variable in size and [illegible], having irregularly hyperchromatic nuclei. After full development the lesions are [illegible] squamous carcinoma. Senile keratoses may possess Bowen's disease structure.



Fig. 922.



Fig. 923.

Fig. 922.—Superficial basal cell epitheliomas in a psoriatic, long previously treated with Fowler' solution.

Fig. 923.—Superficial carcinomatosis in a farmer from arsenic absorbed from sprays. The ulcerative carcinoma over the scapula eventually was fatal.





Figs. 924 and 925.—Superficial basal-cell carcinoma.

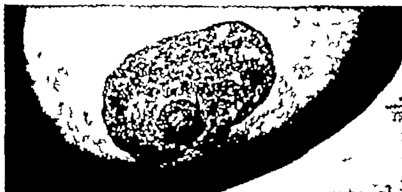


Fig. 326.—Intraepithelial carcinoma of areola and nipple, Bowen's type



Fig. 327



Fig. 328.

Fig. 327.—Paget's carcinoma of the breast. (Dr [illegible])

Fig. 328.—Paget's intraepidermal carcinoma. Hydropic cells permeate epidermis, ducts of the nipple, and body of the mammary gland. Patient soon died with hepatic metastases composed of this kind of cells.



Fig. 329.—Dermatitis of areola resembling Paget disease, from which was cultivated only Staph aureus. Patient was cured by gentian violet.

To cure requires adequate destruction suitable for carcinoma at the moment superficial in location.

**Paget's Disease.**—All of Paget's cases occurred in women between 40 and 60 years of age, and involved the region of the nipple. Males also are attacked, and the disease is not confined to the mammary region. It commences insidiously as sharply circumscribed, eczematous inflammation of the nipple and contiguous areola, or other locale. There may be slight scaling at first. Later the exudation of sticky viscid fluid leads to more or less crusting. Itching is an early symptom. The lesion does not respond to treatment for inflammation and never heals spontaneously. The plaque is sharply defined, and densely infiltrated. The cancer cells are hydropic and noncoherent, spreading intraepidermally in small groups or even singly. They gradually extend peripherally and deep along the ducts, metastasizing early. In Paget's disease of the nipple amputation of the breast should be performed at once.

Paget's disease is a biologic process of symbiosis of epidermal cells and cancer cells; Paget's cancer cells are large sharply defined uninucleated cells with deeply staining nuclei, and retracted, faintly-staining protoplasm (Muir: JPathBact 49: 299 1939). Clinicians sometimes debate whether Paget's disease occurs elsewhere than on the breast, and which of the possible sites of inception the title should be applied to: in the breast with extension outward through the nipple and over the areola; in the nipple with extension onto the skin and into the breast; or in the skin with extension through the nipple into the ducts. Such argument seems trivial to the histologist who sees the same process of intraepidermal carcinomatosis constituting eczematoid neoplastic disease on the lip, in occasional senile keratoses, and on various parts of the body. See Sutton (ADS 46: 1 194) regarding varieties of neoplasia dependent on rate of growth and coherence of parenchyma; also Inglis (Paget's Disease, Oxford U Press, 1936).

Carcinoma in situ applies in histologic description to neoplastic alteration of epithelium limited to epidermal location. Senile keratoses and early carcinoma are of this nature.

## XERODERMA PIGMENTOSUM

The disease may be summarized as the precocious development of sailors skin, keratoses, and basal and squamous carcinomas. It appears early in life sometimes even before the end of the first year. It is directly associated with exposure to sunlight. The sites of predilection are the exposed surfaces, the face and scalp, neck and forearms, and dorsal surfaces of the hands. The first stage of erythroderma corresponds to the time when the child gets outdoors freely. It is characterized by mottling of the skin, diffuse hyperemia, slight puffiness, and some roughening of the surface. Inflammatory irritation is provoked by actinic exposure. The second stage of reaction follows in the third and fourth years of life; pigmentation becomes more apparent in small frecklelike spots, along with active scaling and with transiently appearing flat warts, while hyperemia and edema diminish. Hyperemia of the conjunctivae becomes pronounced and there is more or less photophobia. The third stage of degeneration is characterized by atrophic, mother-of-pearl-like spots often permeated or margined by dilated capillaries, which appear between the pigmented areas, and by warty lesions which become more numerous and pronounced, some of which in the course of months or years become carcinomas. The stages of erythema, pigmentation, atrophy, and tumor formation may be found side by side, the affected skin resembling an x ray burn. Pigmentation ranges from pale yellow to sepia in color and by coalescence, as well as by de novo appearance, patches of considerable extent may become involved. Sudoral activity is somewhat lessened, but the sebaceous glands are little affected. Atrophic contractures of the nose and mouth are common, and ectropion may result, occasionally with ensuing ulceration of the cornea.

The course of the disease may be rapid and progressive, but usually there are periods of comparative quiescence. The victim may survive for many years, but ultimately he succumbs to carcinoma. Sensitivity to actinic light is demonstrable (Lynch ADS 29 858 1934). Inheritance plays an etiologic role (MacKlin ADS 49 157 1944).

One must treat keratoses as they arise, give vitamin A and keep the patient from exposure to the sun. The patient is a pitiable one indeed.



Fig. 930



Fig. 931.

Fig. 930.—Xeroderma pigmentosum [illegible] trophy, pigmentation, keratoses and carcinoma of exposed sk[illegible] in a boy (Dr J H Shelmire)

Fig. 931.—Proliferation of neoplastic basal cells in xeroderma pigmentosum. (Drs. Cornelius and McGrath)



Fig. 932



Fig. 933.

Fig. 93[illegible] [illegible] [illegible]erstaedt [illegible]

Fig. 933.—Xeroderma pigmentosum with [illegible] macular pigmentation and trophic [illegible] L. Halberstaedt )

## MIXED NEOPLASM

**Myxochondroepitheliomatous Tumors** such as occur commonly in the salivary glands may also be found occasionally on the palate, lip cheek, or gums. Such a lesion is firm, rounded or lobulated, and of slow growth but capable of considerable development. It is usually encapsulated, movable and relatively asymptomatic. It may be excised successfully (Driver ADS 33: 72 1936)

Unusual locations include those occurring, rarely it is true, on the palm, leg, arm, hand, calf, or finger (Simard: AmJCa 33 182 1938) Upper lip cases were reviewed by Eggers (Arch. Path. 26: 348, 1938) Brunschwig (SGO 50: 407 1930) found 11 of the tongue.

The tumors were defined by Harvey et al. (EdinMJ 45 275 1938) as adenomas of the serous and seromucous glands, salivary or lachrymal, of undifferentiated and gland lobular types, prone to mucoid, autolytic, self-destructive change of their component tissues. The cells exhibit epidermoid characters both as basal cells and as squamous ones with intercellular bridges and keratinization. Certain aspects of the varied cellular appearance of these tumors led in times past to their being interpreted as endotheliomatous, cylindromatous, chondromatous, basaliomatous, carcinomatous, and even sarcomatous. The tendency of the epithelium and stroma to show myxoid, hyaline, and chondroid transformation gives the tumor its special character and mixed designation.



Fig. 934.



Fig. 935.

Fig 934.—Mixed tumor of pal te. (Abahler ADS 32 622, 1935.)
Fig. 935.—Mixed tumor of parotid, uncommonly large.

**Mucous Gland Tumors in the Skin**, rare, occur occasionally in the skin near the ear in the neck, in the upper sternal area, and about the male urethra, especially along the raphe. The structure is that of simple adenoma of a mucous gland. The lesions are small and they may ooze or form vesicles which rupture (Glasberg and Reuter: ADS 39 5_, 1939) Exc sion cures.

## SARCOMA OF THE SKIN

**Sarcoma** is a malignancy primary in mesodermal cells. Sarcomas may be composed of tissues which sufficiently simulate normal tissues to permit of recognition and to these the names angiosarcoma, fibrosarcoma, and similar terms are applied according to the type of tissue present Others are undifferentiated and are named in accordance with the form of the cells as seen histologically spindle-cell, round-cell mixed cell, giant-cell sarcoma, with subdivision as to size of the cells, large, or small. Pigmented malignancies of melanophores are classed as melanomas, and sarcomatous neoplasms of hematopoietic, lymphatic, and reticular tissues are discussed as lymphoblastomas. See elsewhere in this volume, liposarcoma, rhabdomyosarcoma, hemangioendothelioma, melanoma, neurofibroma with sarcomatous degeneration, and metastatic tumors in the skin.

**Primary Sarcoma of the Skin** is characterized by the occurrence of a localized, round, pea to lemon size, pinkish reddish or purplish tumor which is likely to have developed in some preexisting nevoid excrescence or at the site of an injury The growth may be slightly or considerably elevated above the general level of the skin either as a diffuse, infiltrated tumor or as



Fig. 836.



Fig. 837

Fig. 836.—Dermatofibrosarcoma of dorsolumbar region. (Drs. Hazen and O'Donnell.)

Fig. 837.—Fibrosarcoma of skin (Dr O J Costa)



Fig. 838.



Fig. 839.

Fig 838 —Fibrosarcoma of the back

Fig 839 —Fibrosarcoma showing spindle cells (Dr Stuart W.)

a mushroom like or pedunculated mass The lesions are usually soft and compressible or even pulsatile their consistency differing in accordance with the amount of vascular tissue present The tumors may develop at any age in either sex. The lesions tend to grow expansively so that they possess a sort of capsule The cells are aggregated upon the blood vessels of the stroma, as a rule and tend to metastasize by way of the blood stream.

**Fibrosarcoma of the Skin (Progressive and Recurrent Dermatofibrosarcoma)**.—Small, hard infiltrating nodules develop in the cutis and hypoderm and these increase in size and number slowly to form a dense bluish sclerotic plaque. After a variable but usually long period there appears on this plaque a number of projecting nodules and tumors which may be stalked, may have broad bases or may be pedunculated or sessile (Senear et al. ADS 17 821 1928). In contradistinction to the slow growth of the early fibrous nodules, these tumors enlarge rapidly, often reaching the size of a small apple within a few months. They are hard, as a rule, but may soften later, particularly when the epidermis covering them becomes eroded. They are whitish or purplish, and when their surface becomes eroded, they may develop a tomatolike vegetating appearance. Prompt recurrence with advancing rapidity of growth is the rule after their incomplete removal, and all methods of treatment fail except complete excision if this is performed sufficiently early. The large majority of the cases occur in women. A map of their distribution suggests origin in mammary ridge (Binkley ADS 40 578, 1939).

**Etiology, Pathology and Treatment.**—The role of trauma and irritation is postulated, but the cause is little understood. Some chemical agents, carcinogenic when applied to epithelium, provoke sarcoma when introduced beneath the skin. Benzopyrene injected into the spleens of 96 mice resulted in the development of monocytic leukemia in 9 instances and other sarcomas in 4, reported Furth et al. (AmJCa 31 276 1937). These authors succeeded in inoculating leukemia by the transference of a single cell. Sarcoma has occasionally developed in x ray burns (Burgess ADS 41 407 1940; Denticke BeitrKlinChir 169 214 1939), although such cases may have been in reality spindle cell carcinomas (q v). Accidental autogenous transplantation of a fibrosarcoma in the course of accomplishing a skin graft was reported by Harrell and Valk (AnnSurg 111 285 1940). Grading of malignancy of fibrosarcomas was undertaken by Broders (SGO 69 267 1939), who judged fibrogenic and cellular spindle cell sarcomas as forming distinct groups. The former appear in older patients, the latter are more malignant. The degree of malignancy varies with the number of mitotic figures and tumor giant cells.

The tumors differ greatly in their radiosensitivity and are generally to be treated by radical surgical attack if metastases are not already demonstrable. Surgery, if adequate, may cure even after failure of an initial effort (Bigger SMJ 40 392, 1947). Recurrence increases the danger of metastasis, for this occurred in only 6 primary cases but in 28 of those which had already locally recurred, according to Warren and Sommers (ASurg 33 423 1936).

## MULTIPLE HEMORRHAGIC SARCOMA OF KAPOSI

**Symptoms.** Several lesions usually develop simultaneously, the limbs being the sites of predilection. The early manifestations may take the form of ill-defined, doughy, infiltrated areas, or of collections of several firm, bean to pea size reddish or purplish nodules, often with accompanying telangiectases. The course of these lesions is erratic; they may persist unchanged for months, or ulcerate, or disappear spontaneously. New growths constantly spring up, however, and in a few months the involved parts, especially the legs, become greatly enlarged, the skin being rugous and nodular and bluish or purplish in hue. Symptoms are usually slight.

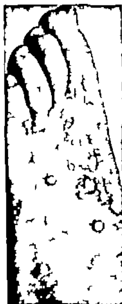


Fig. 940.



Fig. 941.

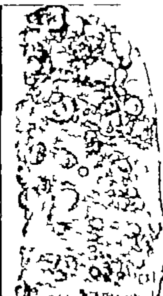


Fig. 942.

Fig. 940.—Kaposi sarcoma (Dr H ward Fox.)
Figs 941 and 942.—Kaposi sarcoma, lesions of feet (Dr L. Halberstaedter)

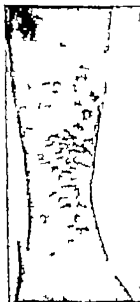


Fig 943.

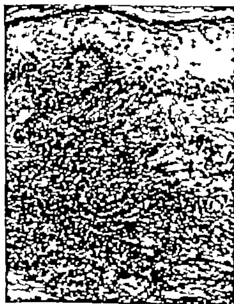


Fig. 944.

Fig. 943.—Kaposi sarcoma. (Dr Howard Fox.)

Fig. 944.—Kaposi sarcoma newly formed vessels with endothelial linings, edema, and pigment granules. (Dr Harold N. Cole.)

The nodules and plaques may be tender or pruritic. Visceral involvement may cause hemorrhage, diarrhea, and other constitutional symptoms. Necropsies have shown that the disease may affect almost every organ of the body

Ordinarily the course of Kaposi s sarcoma is slow and steadily or intermittently progressive. It may be rapidly progressive. The duration varies from 1 to 25 years. Death generally is attributable to hemorrhage and progressive emaciation secondary to extensive visceral involvement.

**Etiology and Pathology.**—The cause is *unknown*. Pigment seems to result from the disintegration of blood, following capillary hemorrhage. The lesions beginning in the skin simulate angiomas, with proliferation and dilation of the blood capillaries. This is followed by proliferation of the interstitial connective tissue and endothelium. The infiltrations resemble in some areas young connective tissue, in other areas, sarcoma. As the lesions grow older they assume a more fibrous aspect and may undergo involution.

Originally described by Kaposi (AfDuS 4 265 1872) important reviews have appeared by Dörffel (ADS 26 608, 1932) and Choisser and Ramsey (AmJPath 15 155 1939) Among the 600 cases of the latter authors were 2 primary in the right heart and lacking skin lesions. Visceral metastases occurred in about 10 per cent; peak incidence was in the 5th, 6th and 7th decades males were affected about 15 times as commonly as females no parasitic etiologic agent has ever been found although the occasional spontaneous regressions are curious if the lesion is blastomatous hematopoietic variations have ranged from lymphocytosis to frank lymphatic leukemia and mycosis fungoides and theories of origin have ranged through infectious granuloma, infection with neoplastic changes supervening neoplasia, and reticuloendothelial hyperplasia. Choisser and Ramsey (SMJ 33 392, 1940) favored the neoplastic theory considering the lesion an angioreticuloendothelioma.

Visceral lesions, hepatic renal, intestinal and mediastinal, especially concerned Tedeschi et al. (APath 53 335 1947) who attributed the variety of manifestations to the multiple developmental potentialities of the reticulum cell as the basic unit of the growth. Sachs et al. (JInvD 8 317 1947) thought of Kaposi s disease as a systemic angiosarcomatosis and exhibited color plates of the histologic findings of new blood vessels, lymphangioendothelium, connective tissue hyperplasia, hemorrhage, and cellular infiltration comprising small round cells, wandering connective tissue elements, plasma cells, angioblasts, spindle cells, and fibroblasts. Any of these features may predominate, so that one section may simulate angioma, granuloma, inflammation or malignant sarcoma but vascular hyperplasia, hemorrhage, angioblasts, and spindle cells are constant. The spindle cells grown in tissue cultures of explants by Becker and Thatcher (JInvD 1 379 1938) were not fibroblasts.

**Treatment.**—X ray therapy proves helpful, and radium too may be used. Recovery has apparently occasionally followed hypodermic injections of sodium cacodylate Cases treated at Radiumhemmet solely by irradiation (Hansson abs ADS 44 1119 1941) appeared to justify hopeful prognosis, for only 7 of 23 died and their deaths were not certainly due to Kaposi s disease However hemorrhage from a visceral metastasis caused death in a patient of Aergerter and Peale (APath 34 413, 1942)

## DISEASES PRESUMABLY SARCOMATOUS OF THE HEMATOPOIETIC SYSTEM AS SEEN IN THE SKIN

**Introduction.**— The origin of the leukocytes is thought to be in the primitive reticulum cells, from which maturative steps lead to 3 distinctively different kinds of cells, lymphoblasts, myeloblasts and monoblasts, from which in turn are formed lymphocytes, myelocytes and monocytes, wrote Andrews (Dis. of Skin, Saunders, 1946)

Some hematologists believe that, in addition, cells of the reticulo-endothelial system which are derived directly from this syncytium retain their hematopoietic ability to produce cells of the lymphoid, myeloid or monocytic series. Two kinds of hematopoietic diseases result from hyperplasias of these cells. Leukemia is a growth of these cells in the circulating blood, with a decrease in the maturation of the cells, being designated lymphatic leukemia, myelogenous leukemia or monocytic leukemia according to the variety of proliferation. Another form of hematopoietic disease is characterized *by the proliferation of these cells within* the tissues without leukemic changes in the blood. To the latter group the terms aleukemic leukemia, aleukemic myelosis and aleukemic reticulosis (or aleukemic reticuloendotheliosis) are applied. As combinations of all of the previously mentioned forms occur it is natural that some confusion exists in the classification of these processes. The term lymphoblastoma includes several diseases of lymphatic origin, but myeloid and monocytic leukemia, reticuloendotheliosis and mycosis fungoides are not properly included in it. In a small group of cases of leukemia, blood smears may show unusual cells which resemble not only monocytes but also lymphocytes, myeloblasts plasma cells and reticuloendothelial cells. To this disorder Ewald gave the name leukemic reticuloendotheliosis, which term is also applied to monocytic leukemia. The former is regarded by many as a subleukemic form of the latter. Likewise aleukemic reticuloendotheliosis is regarded as the aleukemic manifestation of monocytic leukemia. The present tendency is to emphasize the genetic relationship of these various diseases, but there are essential differences as well as similarities. Cases are reported in which at one phase of the disease the clinical and hematologic picture is of lymphatic leukemia, at another stage that of mycosis fungoides, or at some other stage some other type of lymphoblastoma. In other cases there have been simultaneous developments of leukemia and reticuloendothelial reactions, such as in Kaposi's hemorrhagic sarcoma. Infiltration of the skin with hyperplastic hematopoietic tissue occurs most frequently in the affections commonly designated lymphatic leukemia, mycosis fungoides and lymphosarcoma, less often in myelogenous or monocytic leukemia, Hodgkin's disease and in other members of the hematopoietic group of diseases.

Tumors involving the hematopoietic tissues may affect the skin primarily or secondarily. Their component cells may like tumors of other tissues, resemble a normal type of cell with sufficient similarity to justify specific tissue diagnoses, such as lymphocytic, myeloid, or monocytic processes. The cells of the tumors may remain fixed in their sites of proliferation, or they may circulate, and the diagnosis is thus to be qualified as aleukemic or leukemic. A process at one time aleukemic may become leukemic, or vice versa, or the extent of leukemia may vary greatly during the course of the disease.

It is debatable whether the processes designated as leukemia, aleukemic leukemia, lymphosarcoma Hodgkin's disease, mycosis fungoides and the

like are in fact sarcomas, but Warthin (AnnSurg 93 153, 1931) argued, There is no inflammation in these neoplasms, all the patients are dead, the course is inevitably fatal, they spread by infiltration they have all the characteristics of neoplastic overgrowth and none of an infectious process. Keim (ADS 19 533 1929) concluded after a study of many cases of leukemia, mycosis fungoides, lymphosarcoma, and Hodgkin s disease that these disorders are genetically related pathologically and might profitably be grouped under one heading lymphoblastoma.

**Classification.**—That of Robb-Smith (JPathBact 47 457 1938) merits careful study see reticular sarcoma p 656 Krumbhaar (J 106: 286 *1936*) listed myelogenous, lymphogenous, and reticulogenous neoplasias as follows

| | MYELOGENOUS | LYMPHOCYTIC | RETICULAR |
|---|---|---|---|
| Tissue hyperplasia and leukemia | Acute or chronic myelogenous leukemia (leukemic myelosis) | Acute or chronic lymphocytic leukemia (leukemic lymphadenosis) | Monoblastic leukemia (leukemic reticulosis) monocytic leukemia |
| Aleukemic variety *of hyperplasia* | Acute or chronic aleukemic myelosis | Acute or chronic aleukemic lymphadenosis | Aleukemic reticulosis |
| Malignant tissue changes only | Myelogenous myeloma aleukemic myelochloroma | Lymphosarcoma; lymphoid myeloma; plasma cell myeloma; lymphochloroma | Reticulum cell (retothelial) sarcoma |

**Skin Lesions.**—The study of 445 cases by Epstein and MacEachern (AIntM 60 867 1937) showed that the skin was involved as follows

| | HODGKIN'S DISEASE | LYMPHOSARCOMA | MYELOID LEUKEMIA | LYMPHATIC LEUKEMIA | ACUTE LEUKEMIA | MONOCYTIC LEUKEMIA |
|---|---|---|---|---|---|---|
| No. of cases | 156 | 122 | 90 | 60 | 6 | 4 |
| Petechiae | 4 | 4 | 27 | 15 | 3 | 1 |
| Pigmentation | 15 | 2 | 2 | 1 | 0 | 0 |
| Stomatitis | 1 | 3 | 11 | 4 | 1 | 0 |
| Pruritus | 1 | 4 | 0 | 2 | 0 | 0 |
| Maculopapules | 1 | 0 | 3 | 1 | 0 | 0 |
| Herpes zoster | 4 | 1 | 1 | 1 | 0 | 0 |
| Bullae vesicles | 3 | 1 | 5 | 0 | 0 | 0 |
| Furunculosis | 0 | 1 | | 1 | 0 | 0 |
| *Lichenoid papules* | 0 | 1 | *0* | 1 | 0 | 0 |
| Urticaria | 1 | 0 | 0 | 0 | 0 | 0 |
| Herpes simplex | 1 | 3 | 0 | 0 | 0 | 0 |

There is no sharp dividing line between the so called exanthems and true tumors, Gates (ADS 37 1015 1938) found. Leukemia as tumors with circulating metastases, and lymphoma as tumors which arise in discrete location she thought cannot be differentiated as to cutaneous lesions clinically or pathologically. Mycosis fungoides she considered a type of leukemia or lymphoma with predominating skin tumors. The skin tumors seem to be the result of chance location of diffusely disseminating cells. In some cases sites of injections and surgical incisions have become metastatically infiltrated with leukemic tissue. Zosteriform arrangement of the lesions in leukemia cutis has been seen (Barney ADS 37 235 1938). Dermal infiltrations with many kinds of cells originating in undifferentiated reticulum were summarized by Wehlman and Custer (abs YBD 1937 p. 320)

## SKIN LESIONS IN CIRCULATING-CELL MESENCHYMAL BLASTOMA

The skin lesions of leukemia cutis may be clinically indistinguishable from those occurring in purpura, prurigo and other cutaneous disorders, or they may be typically lymphadenotic in character. Purpuric skin manifestations may or may not include formation of bullae and may involve the mucous membranes as well as the skin, especially in acute monocytic leukemia, where bleeding, swelling of alveolar ridges, mandibular pain, and ulcerative and gangrenous gingivitis are seen in perhaps half the cases (Moloney NEngJM 222: 577 1940; Hubler and Netherton ADS 56: 70 1947). Pigmentation may be Addisonian. The 3 types of specific skin lesions comprise (1) leukemids, (2) erythrodermic infiltration of the skin with tumor cells and (3) circumscribed tumor formation.

**Lymphatic Leukemia With Skin Lesions.**—The tumors, usually numerous but occasionally solitary, commonly appear with the eruption of a number of small papules, and these increase slowly in size and number. Erythematous macules and slightly indurated plaques are common. In many cases diffuse though not completely generalized swelling of the skin is associated with discrete cutaneous tumors. Extensive ulceration may occur. Erythrodermic lymphatic leukemia is occasionally primary in the skin before visceral involvement.



Fig. 945.—Leukemia: reddish brown nodules in skin. (Dr John Butler.)

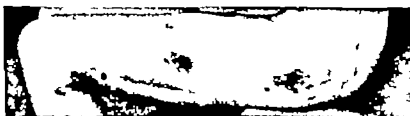


Fig. 946.—Leukemic lesions with ulceration, thigh. (Dr A. B. Cannon.)

**Myelogenous Leukemia With Skin Lesions.**—Lesions include specific tumors (leukemids), erythroderma, bullous eruptions, and rosacea-like eruptions. The appearance of cutaneous manifestations in chronic myeloid leukemia presages the terminal phase. See Hellander et al. (ADS 29: 821 1934); Paul and Linnard (ib. 45: 597 194_.)

**Monocytic Leukemia.**—Griffin and Watkins (AmJMSc 188: 761, 1934) separated the Naegeli type, a variant of myeloid leukemia with predominance of monocytes, from the Schilling type, which is a leukemic reticuloendotheliosis (Montgomery and Watkins: ArIntM 60: 51, 1937). Either may begin primarily in the skin. Mercer (ADS 31: 615, 1935) collected some 51 cases of monocytic disease among which his two patients exhibited diffuse exanthems of slightly red macules changing to slate blue, also firm, pale papules, a few large nodules and some lesions purpuric in appearance which on section were actually leukemids. Eight cases, with ulceration, were described by Lynch (ADS 34: 775, 1936). Montgomery and Watkins (MinnM 1: 636, 1938) reported 4 with exfoliative dermatitis, in which type ulcerative gingivitis is not common. The eruption seemed typical to Freeman and Kolетsky (ADS 40: 218 1939) in that it begins maculopapular simulating secondary syphilis, and evolves from day to day in areas sometimes



Fig. 947



Fig. 948.

Fig. 947.—Myeloid leukemia. (Ketron and Gay ADS 7 176, 1923.)
Fig. 948.—Hodgkin disease, cutaneous infiltration. (Dr D. H. H. Cleveland.)



Fig. 949.



Fig. 950

Fig. 949.—Leukemic nodule in skin.
Fig. 950.—Monocytic leukemia, cutaneous lesion encircled cells show folded bean appearance typical of monocytes. (Loveman SMJ 29: 387, 1936.)

disappearing. Necrosis of the skin especially at the folds, and the change from aleukemic to leukemic with a total white count perhaps less than 20,000 are ominous, and the course is sometimes fulminating (Herbut and Miller: AmJPath 23: 93, 1947). Swelling of the gums occurs in 80 per cent and may be the first symptom. Lymph node and splenic enlargement are not extreme when present. Pallor weakness, low fever and bone and joint pains are common accompaniments. Monocytic leukemia is accompanied by skin lesions in about 60 per cent of the cases. Purpura and hemorrhagic and bullous lesions seem to be common early in monocytic leukemia.

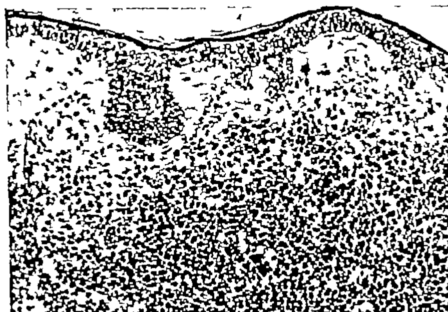


Fig. 951.—Myeloid leukemia, cutaneous nodule. (Dr Lloyd Ketron)

## SKIN LESIONS IN DISCRETE HEMATOPOIETIC BLASTOMAS

**Lymphoma.**—The cutaneous tumors of lymphoid hyperplasia are more apt to be large, ulcerated and fungating and are somewhat less stable than the tumors accompanying leukemia. Single tumors are more common than in association with leukemia but are relatively infrequent. Diffuse infiltration and plaques occur, as well as discrete tumors. In the majority of cases lymphoma is of the Hodgkin's disease type. See Brill et al. (J 84: 668, 1925), Gates (ADS 37: 1015, 1938) Combes and Bluefarb (Ib. 44: 409 1941) Gall and Mallory (AmJPath 18 381, 1942)

**Giant Follicular Lymphadenopathy** (Brill-Symmers) clinically strongly resembles Hodgkin's disease and is usually mistaken for it (Uhlmann Radiol 50 147 1948) It is characterized by local or general enlargement of the lymph nodes, often in conjunction with splenomegaly The nodes are relatively soft and the patient well being is not greatly influenced. Histologically the masses suggest lymphoid hyperplasia or chronic lymphadenitis. While small doses of radiation suffice to induce most nodes to disappear Uhlmann thought it advisable to treat the disease as potentially malignant, using intensive therapy intended to prevent the development of Hodgkin disease, leukemia, and sarcoma.

**Lymphocytoma** is the most benign form of lymphoblastomatoid tumor The lesions are characteristically composed of papulonodules of various dimensions, often symmetric in location, red, brown or violet in color, and slow in evolution. The surface is smooth. The locations are the face, the lobes of the ears, the scrotum, rarely the extremities. See Moescher (abs ADS 38 841 1938) Hallam and Vickers (BJD 51: 233, 1939) Heller (BJD 51 260 1939)



Fig. 952.



Fig. 953.

Fig. 952.—Lymphocytoma (Hiller BJD 51 260 1939)
Fig. 953.—Lymphocytoma in a woman 46 years old.

Fig. 954 Fig. 955 Fig. 956.

Fig. 954.—Leukemic nodules in skin of ear
Fig. 955.—Exfoliative dermatitis of legs in Hodgkin disease (Berrack J 126: 1023 1944.)
Fig. 956.—Hodgkin disease cutaneous infiltration. (Dr Henry Michelson.)

**Spiegler-Fendt Disease**, described as a "sarcoid" because of the formerly het erogeneous connotation of the term, is thought to belong to the hematopoietic blastoma group (Lewis: ADS 31: 67 1935) Spiegler (AfDuS 7: 163 1894) and Fendt (ib. 53: 213, 1900) excluded metastatic tumors in the skin and mycosis fungoides from their entity which Kaposi thought formed a clinically fairly characteristic picture of multiple skin tumors. These are firm, elastic, globular situated in the dermis and beneath it, not progressive beyond a certain stage of enlargement and sometimes involuting spontaneously They are not associated with lymph node or hematologic changes. Arsenic cured or improved the patients. Lewis distinguished the localized, superficial type from the multiple disseminated, collecting 11 examples of the former and 22 of the latter Ages ranged from 5 to 76 years; sex predilection was not apparent; and the color of the lesions ranged through red, purplish, and brown, the number from 1 to 200 the consistency soft to firm and the size from millet seed to walnut, with solitary plaques occasionally noted.

Histologically the lesions are difficult to distinguish from skin nodules of lymphatic leukemia. Their difference from lymphocytoma is doubtful (Bafverstedt: also ADS 53: 186, 1946)

They are radiosensitive responding to a dose or two of 125 to 200 r (Cipollaro: ADS 53: 166, 1946) The case of Sweitzer (ADS 11 481, 1925) a disseminated one involuted under x ray therapy relapsed and died of cachexia with numerous shotty papules in the skin and a large nodule in the kidney

**Reticular Sarcoma.**—Robb-Smith (JPathBact 47: 457 1938) distinguished reticulosis and reticulosarcoma. Any variant may or may not manifest circulating cells. The sarcomas may show (1) undifferentiation (diffuse or trabecular) (2) histoid differentiation (dictyosyncytial or dictyocytic) (3) hemic cell differentiation (lymphocytic, lymphosarcomatous, myeloblastic, plasmocytic, monocytic or erythroblastic) (4) differentiation like the cells which line lymph sinuses, and finally (5) mixed types. Robb-Smith (BJD 56: 151 1944) simplified his classification of reticulosarcomas into the hemic (lymphosarcoma, chloroma, plasma cell myeloma) and histioid types. In the latter the formation of reticulin is characteristic. Reticulin, collagen, and elastica together comprise the 3 types of fibers in the dermis; recognition of reticulum histologically was clarified by Robb-Smith (BMBull 3 172, 1945) The many variations of cell type depend on the potentialities for differentiation of the reticular cells. Leukemia is much more common in the hemic varieties.

Nodular infiltrated and indurated lesions of the axillae and groins were observed in one woman, the cells resembling those of primitive mesenchymal syncytial reticulum of lymph sinuses. Violently progressive soft, fungating, radioresistant sarcomas of this kind, without leukemia, are occasionally seen. The 36 year-old male reported by Wayson and Weidman (ADS 34 735, 1936) exhibited a rapid clinical course without leukemia and with skin changes like those of premycotic and later tumorous mycosis fungoides. The diagnostic requirement of sternal puncture and bone marrow study in such cases is apparent.

**Hodgkin's Disease** may give rise to skin lesions, particularly papules and nodules clinically indistinguishable from those of leukemia cutis. Skin changes occur in some 25 per cent of the cases; in 5 to 12 per cent the skin changes come first (Cole: J 69 341, 1917) The commonest manifestation is pruritus, with or without signs of the general disease; the itching tends to become exacerbated with involvement of fresh nodes. A prurigo-like exanthem on the extensor surfaces or generally disseminated may come and go for months. Urticaria is common, but exfoliative erythroderma is rare. Pigmentation is usual and may be spotty or diffuse sometimes Addisonian, but it leaves the mucosae free. Alopecia and dryness, atrophy and hyperkeratosis of the skin are seen. Icterus may occur Finally the primary tumors may rise in the skin (Senear and Caro: ADS 35: 114, 1937) The first lesion may be a solitary skin tumor which ulcerates, like that reported by Pessin and Pohle (AmJCa 34 229, 1938) While lymph node hypertrophy is the invariable manifestation of Hodgkin's disease, the cardinal diagnostic symptoms of Colrat, splenic and lymph node hypertrophy fever pruritus, progressive anemia, and increasing polymorphonuclear leucocytosis, are not frequently all present, according to Cleveland (CanadMAJ 56 614 1947)

Some 30 to 40 per cent of cases show skin symptoms, including pruritus, nodules, rarely exfoliative dermatitis, and herpes zoster due to ganglion involvement, but mucosae remain free and tonsils are not involved as they are in other lymphoblastomas, reported Goldman (J 114 1611 1940) in a review of 21. cases. The ichthyosiform change often seen may be due to liver damage and resultant malmetabolism of vitamin A (Glassbrook and Tomaszewski ADS 50 85 1944) Desjardins (J 103 1033, 1934) called attention to the frequency with which the first nodes affected are those draining a site of chronic

p.o. daily, 25 mg intramuscularly weekly. Sigel (ib. 5: 1?, 1945): 3 cases in Negroes; Levin and Behrman (ib. 51: 307, 1945): x-ray therapy, consideration of skin dose, avoid arsenic. O'Leary (ib. 54: 585, 1946): benefit with chaulmoogra oil, 2 to 6 c.c. daily × 30 while patient receives 5 to 8 fever treatments; deep sunstan maintained for 4 months clears premycotic mycosis fungoides.



Fig. 938.—Mycosis fungoides at site of parapsoriatic lesions. (Dr. Grover Wende.)



Fig. 939.



Fig. 940.

Fig. 939.—Mycosis fungoides, tumor of tongue. (Dr. George M. MacKee.)
Fig. 940.—Mycosis fungoides, early tumors. (Dr. H. M. Robinson.)

**Etiology, Pathology and Diagnosis.**—The cause of lymphoblastoma is unknown. The history and course in some cases suggest an acute infection. Local proliferation occurs in the tumors, as the presence of mitosis attests. In leukemia the infiltration of the skin and the subcutaneous

**Treatment.**—Good results in leukemia have followed the administration of benzene a leucocyte poison. Arsenic may benefit, and arsphenamine, in small doses, has proved beneficial in a few instances. Radiotherapy over skin, lymph nodes, or the long bones may yield excellent results for a time. Substances rendered radioactive by use of the cyclotron are of value when given orally in doses guided by blood findings (Warren NEngJM 223 751 1940). P[32] prolonged comfortable life, and its administration did not produce radiation sickness, but did not result in any marked improvement in longevity in the 129 patients with chronic myeloid leukemia studied by Lawrence et al. (J 136 672, 1946). Transfusions and other palliative efforts are used.

THE NITROGEN MUSTARDS particularly of war gas chemicals, have an action on nucleoprotein resembling that of x rays (Gilman and Philips Sc 103 409 1946). Goodman (J132 127, 1946) reviewed 67 cases treated with such chemicals, and Jacobson et al. (ib. p 263) reported 59 patients with diseases of the hematopoietic system who were given methyl bis (beta-chloroethyl) amine hydrochloride in doses of 0.1 mg per kg in courses of from 1 to 7 daily injections. The margin of safety was narrow and serious toxic effects such as granulocytopenia, thrombocytopenia, and anemia were avoidable by a safe dosage schedule. Less consequential side effects included pain on injection, thrombosis of injected veins, vomiting, malaise, anorexia, and headache. Benefit was greatest in Hodgkin's disease lymphosarcoma, and chronic leukemia, with sometimes dramatic improvement in lymphadenopathy splenomegaly and hepatomegaly. Acute leukemia and multiple myeloma did not respond. Cases no longer responsive to x ray therapy may respond to these chemicals, and relapses after nitrogen mustard treatment have responded to further treatment with the agent. Cure is not obtained, benefits resemble those induced by radiation, and optimum dosage has not been worked out. Utility is especially noteworthy after radioresistance has developed, reported Osborne et al. (J 135: 1123 1947) who used the drug also with benefit in chronic disseminated lupus erythematosus. See Edit. (J 135 98, 1947); Philpott et al. (J 135: 631, 1947); Taffel (YaleJBiol 19: 971 1947) not curative in 16 cases, but beneficial in 1 case of mycosis fungoides; Kierland et al. (JInvD 9: 195, 1947) 6 cases, 4 of which had become radio-resistant, with benefit but some severe reactions; Apthomas and Cullumbine (Lancet 1 899 1947) palliative in 21 cases of Hodgkin's disease. See Wintrobe (AnnIntM 27: 529 1947) on dosage and technic of administration. Toluidine blue intravenously was an effective antidote for the anticoagulant effect of the drugs, reported Smith et al. (Sc. 107: 474 1948). Nitrogen mustards are not useful in early localized forms of lymphoblastoma, where radiation in about the maximum dose the skin can tolerate was preferred by Craver (J 136: 44, 1948). He estimated that even when Hodgkin's disease or lymphosarcoma begins to generalize by and large roentgen irradiation is a more effective agent than any of the nitrogen mustards that have been tried.

## METASTATIC TUMORS IN THE SKIN

**Secondary Neoplastic Infiltrations in the Skin** are of considerable diagnostic interest (Willis The Spread of Tumours, J & A. Churchill, 1934). Metastases may reach the skin by (1) invasion by extension via tissue blood and lymph spaces, (2) lymphatic embolism, and (3) hemic embolism.

**Invasion** is exemplified most commonly by mammary cancer and by growths in the cervical or inguinal lymph nodes. By stretching and thinning the dermis may long resist perforation. When this occurs, exuberant fungation is the rule. Cancers originating in the mouth, cervix uteri, larynx, and penis and melanomas, may produce similar satellites. Outcrop nodules, often lentiform or plaquelike are frequent in the skin in the neighborhood of mammary cancer. Extension via vascular channels may consist in inconspicuous permeation, or in redness, tenseness, and burning sensations as in inflammatory carcinoma of the breast,



Fig. 944.



Fig. 945.

Fig. 944.—Carcinoma en cuirasse with lenticular outcrop nodules and lymphedema of left arm. (Dr Howard Morrow)

Fig. 945.—Inflammatory carcinoma of breast, extremely rapid in progress.



Fig. 946.



Fig. 947

Fig. 946—Squamous carcinoma in wen, with metastases in scalp and lymph nodes.

Fig. 947—Outcrop nodules of buttock, carcinoma of rectum. (Dr. T W Allworthy)

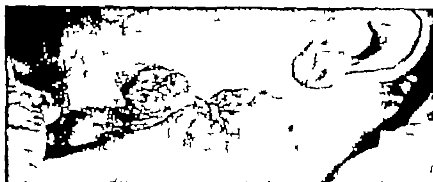


Fig. 968.—Recurrence of squamous carcinoma in area of operation intended to remove cervical lymph node metastases of cancer of the lip.



Fig. 969.



Fig. 970.

Fig. 969.—Hematogenous metastases of hypernephroma. (Dr. Sam Sweitzer.)
Fig. 970.—Metastasis from prostatic primary. (Ronchese: ADS 41: 439, 1940.)



Fig. 971.—Metastasis of [illegible] breast carcinoma into [illegible] lymph [illegible] of the skin. Carcinoma [illegible] the [illegible] endothelium-lined spaces. (Dawson and Shaw: BJD 25: 100, 1937.)

or in nodules or plaques formed by outcropping of the permeations of the deep fascial plexus, or in cancer en cuirasse (Reuter and Nomland WiscMJ 40: 196, 1941) Carcinoma en cuirasse may be manifested by small, flattish papules usually rising slightly above the niveau, carcinoma lenticulare Discrete at first they coalesce to form leathery induration The commencement may be morphea like, or marbling may appear with only slight induration. Progress is slow but the telangiectatic type may go fast (Savatard BJD 65 31 1942) and the erysipelas like, fulminating cases are due to invasion of blood channels by tumor cells (Dawson and Davie EdinMJ 49: 247 1942)

Lymphatic obstruction may give rise to edematous elephantiasis of the part. Gangrene of the skin may result.

**Lymphatic Embolism** is probably the usual way in which carcinoma and melanoma cells reach the regional lymph nodes. This is the only route that is important in operable cases of carcinoma (Gray BJS 26 462, 1939) and melanoma.

**Hematogenous Skin Metastases** are not likely to be present until extensive visceral metastasis has already taken place The incidence of skin secondaries was 2.7 per cent in 2,300 autopsies reviewed by Gates (AmJCa 30 718, 1937) Of the epithelial growths, half had originated in the breast. No tumor she thought, shows real predilection for cutaneous metastasis. Skin lesions of hematopoietic blastomas (q v ) are usually metastatic lesions, though of course some are primary There is no sharp dividing line between the so-called exanthems and the true cutaneous tumors in the leukemias. These are the result apparently of merely fortuitous localization of diffusely disseminating cells Zosteriform distribution of metastases has been observed. Wenlike lesions of the scalp may in reality be metastases from distant cancerous organs.

Interesting cutaneous phenomena of metastasis have been recorded widespread exudative rashes even exfoliative dermatitis, from cancer of stomach and of pancreas (Becker et al. ADS 45 1069 1942) macular papular and vesicular lesions universally distributed in a newborn from a thymus primary (Wasserman et al. JPed 14 798, 1939) lesions resembling inflammation affecting the thighs in ovarian cancer (Urbach et al. ADS 43 962, 1941) nodular lesions of the scalp simulating turban tumor prostatic in origin (Ronchese ADS 41 639 1940) subcutaneous nodules usually on the same side as the affected bronchus in pulmonary cancer (Charache AmJCa 37 431 1939) and transplanted tumors in surgical scars, such as those reviewed by Lazarus (AnnSurg) 107 278 1938)

**Prognosis.**—The recognition excision and microscopic examination of metastatic lesions may occasionally first lead to diagnosis of the primary tumor Their prognostic import is obviously grave Death eventuates as a rule within 3 months of the appearance of dermal secondaries arising from the gut. Scalp metastases from a mammary cancer responded favorably to testosterone injections given by Cutler and Schlemenson (J 138 187 1948)

## DISEASES PARTICULARLY AFFECTING THE CUTANEOUS APPENDAGES

### DISORDERS AFFECTING THE HAIR

#### HYPERTRICHOSIS (HIRSUTIES)

**Hypertrichosis**, excessive or abnormal hairiness from any cause may be congenital or acquired. It may be of limited or universal distribution. Hypertrichosis lanuginosa, the universal dog faced type, is extremely rare. Localized heavy growth, particularly in pigmented areas on the lower trunk, buttocks, and thighs, is common and is classified with nevi

Acquired hypertrichosis is a comparatively common disorder The areas commonly affected are the cheeks, chin, and the upper lip and occasionally the forearms and the legs.

Why hair grows is a problem in embryology a field in which problems are pursued but answers are elusive. Under some circumstances a lanugo hair may develop into a large, stiff bristly one. Whether shaving trauma, erythema, munctions, or other local phenomena are pertinent to the change is uncertain. Shaving probably encourages the growth (Hu and Frazier AnatRec 77 155 1940) Various endocrine imbalances greatly influence the growth and distribution of the hair Knowledge of hormones concerned with growth of hair is still so sketchy that therapy based on it is guesswork. Sexual function is related to hair growth. We have seen excess of hair of the upper lip and chin disappear in women following marriage we have seen it make its appearance after divorce. We have seen hirsuties follow thyroidectomy Adrenal cortical and other tumors are capable at times of inducing masculinization and hair growth see under striae distensae, and purpura The syndrome includes obesity of rapid onset, hirsuties, amenorrhea hypertrophy of the clitoris, osteoporosis, and hypertension (Freyberg et al. AIntM 58 187 213 229 1936 Cahill PaMJ 47 655 1944) Long coarse hairs of the ears in Caucasian males indicate that androgenic hormone is or has been adequately supplied (Hamilton Trans Soc. Inv D., 1947) Sex hormone influence on hair growth was studied by Hooker and Pfeiffer (Endocr 32 69 1943); principle effects were on sebaceous glands, estrogen reducing them and androgen promoting their hypertrophy Estrogen perhaps yielded temporary benefit of hirsuties in women in experiments of Dorff (AnnIntM 13 2112, 1940) though its topical application was a failure according to Whitaker et al (JInvD 9 49 1947) Apparent hair growth after death is probably nothing more than increment in its projection as the tissues shrink (QMN J 116 264 1941) Excessive growth on limbs following nerve injury probably results from diminution in the frictional loss to which the hair is normally subjected (see J 114 273 1940)

*The Hair and Scalp* by Savill (Wood, 1945) is an authoritative treatise, and *Diseases of the Hair* by McCarthy (Mosby 1940) is complete and informative, in so far as information exists. See also Danforth (ADS 11 494 637 804 12 76 195 380 628 1925 PhysRev 19 94 1939)

Hairs are generally permanent unless destroyed. Electrolysis is the safest and best means for destroying the follicles.

A direct current of from 1 to 2 milliamperes is used. The slender needle with bulbous tip, is attached to the negative pole. A damp sponge is attached to the positive pole. After the operator gently inserts the needle along the hair shaft to the depth of the follicle, a delicate and tedious task, the patient closes the circuit by touching the sponge with the finger. In from 10 to 20 seconds bubbles appear at the orifice of the follicle, the patient is told to break the circuit, the needle is extracted and the hair, if sufficiently damaged, is readily pulled out. With clean skin and clean needle, infections do not occur. Adjacent hairs are not attacked at one sitting for fear of scarring. From 10 to 60 per cent of the hairs so removed recur. Single needle technic is best. A multiple electrode technic was described by Marton (APhysTh 21: 678 1940).

Roentgen therapy depilates by producing follicular atrophy. *The dose which depilates permanently produces permanent cutaneous damage.* While the agent can be used wisely and helpfully in hairy nevi, perhaps, its dangers and damaging effects were graphically described by Cipollaro and Einhorn (J 135: 349, 1947) and by Cleveland (CanadMAJ 59: 374, 1948). See Robinson (SMJ 40: 619 1947).

The monopolar high frequency technic is fast (Karp ADS 43: 85 1941) but difficult of application and likely to scar (Ellis Ib. 56: 291, 1947).

Chemical depilation can be accomplished with strontium sulfide in an equal amount of a mixture of zinc oxide and starch; mix this with water to form a thick paste, apply liberally, scrape off after 5 to 7 minutes, rinse thoroughly first with water then with a weak acid wash, and apply cold cream and finally talc. Fresh barium sulfide, 33 per cent in zinc oxide and starch, may be used similarly; it is poisonous. Hair may be rubbed off with pumice stone, or bleached, after thorough washing, with 20 volume $H_2O_2$ to which has been added about 5 per cent of ammonia water.

Many a girl, unduly disturbed by hairiness which is not outside the range of normal variability, is best advised to adapt herself psychologically to the cross she must bear.

## ATROPHY OF THE HAIR

This may be either symptomatic or idiopathic. Symptomatic atrophy is generally due to severe constitutional disorders, such as cancer, tuberculosis, diabetes, or avitaminosis, and it may occur as a result of a local disorder such as tinea or seborrheic dermatitis. It is characterized by dryness, splitting, and curling of the affected shafts, with loss of flexibility. The idiopathic form is a manifestation of ectodermal defect (p. 671) and 3 varieties are described.

Fragilitas Crinium may manifest itself by splitting or breaking of the shaft. Excessive washing, low humidity, hypothyroidism, and diets lacking in vitamin A are factors likely to be concerned. The patient complains that the hair is abnormal to the touch and seems to be parasitized by creatures she wishes to pick off or to brush out, and brushing the hair actually results in further splitting of its feathered ends.

Trichorrhexis Nodosa is a peculiar nodose condition of the hair characterized by longitudinal splitting at intervals along the shaft, the formation resembling two small, round brushes pressed end to end. The disease gives rise to little actual hair loss. If a hair consists of cells of brittle maturation through nutritional influences, an abrupt angulation of the cylindric shaft by mechanical influences probably occasions a nodose splintered fracture. Vitamin A concentrates might be tried, and fat solvents should be avoided. Familial cases are seen.

Monilethrix, beaded hair, is an anomaly usually congenital and frequently hereditary which is characterized by fusiform swellings separated by atrophic constrictions so that the affected filament presents a beaded appearance. The shafts are fragile and break readily at the internodal constrictions, so that extensive alopecia is common. Keratosis pilaris is often present. The disease is usually confined to the scalp (MacKee and Hesse JCutDis 34: 444, 1916). Vitamin A is helpful. Appel and Messina (NEngJM 226: 912 1942) described an affected sibship, whose disorder they thought an ectodermal dysplasia. The boy reported by Clarke and Glickstein (ADS 43: 836, 1941) lacked hair until age 4.

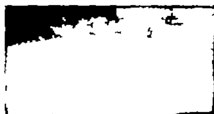


Fig. 972.



Fig. 973



Fig. 974

Fig. 972.—Hypertrichosis.

Fig. 973.—Hirsuties associated with masculinizing ovarian blastoma. (Rottino and McGrath, Arch. Int. Med. 63: 686, 1939.)

Fig. 974.—Masculinovoblastoma, skin changes. (Drs. Rottino and McGrath.)

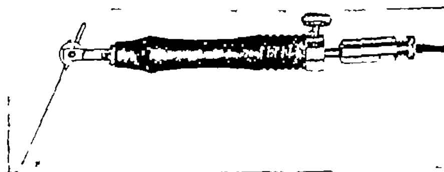


Fig. 975.—Needle and holder for electrolysis. (Dr. H. C. [illegible].)



Fig. 976.—Monilethrix. (Drs George MacKee and Isado Rosen.)

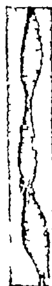


Fig. 977




Fig. 978



Fig. 979.

Fig. 977.—Monilethrix. (Dr. J. F. [illegible])

Fig. 978.—T[illegible] (1 and 2) compared with monilethrix (3). (Ronchese, ADS [illegible] 1932.)

Fig. 979.—T[illegible] nodosa. (Dr. Fred Weidman.)

## INGROWING HAIR

It is common for one or several hairs of the beard to be set obliquely and to pierce the epidermis of the follicular walls. They may not penetrate the corneum at all, but grow beneath it. Such buried hairs cause small papules, which may suppurate. These generally heal without scar Close shaving may predispose to their appearance; but ingrowing hairs affect some individuals and are not found in others. Beards of men are almost the exclusive site

Tiny glassy asymptomatic papules containing fine black hairs are often seen on the legs and thighs. The hairs are doubled over and can readily be picked out as wiry loops, constituting a disturbance which may be coincidental with, or actually a manifestation of keratosis pilaris (see p. 567)

Papules containing ingrowing hairs should be pricked and the hair pulled out, using clean hands and clean instruments, and touching the wound afterward with a suitable antiseptic (QMN J 119: 534, 1942)

**Scarring Pseudofolliculitis of the Beard in Negroes (Folliculitis Barbae Traumatica)** has been accurately reviewed and investigated by Greenbaum (ADS 21: 237 1935) and Pincus (ADS 47 783, 48: 539 1943) In the Negro the curl of the hair results in its curving back into the skin after emergence from the follicle so that foreign body inflammation and eventual scarring develop The hairs come to lie in shallow grooves which persist as narrow crimerous scars when the hairs degenerate. In treatment, close frequent shaving may be advised, and temporary epilation with x-rays may help.

## CANITIES

**Grayness of the Hair** occurs in several forms

Congenital Whiteness of the Hair is rarely complete, but it occurs in albinism (q. ) and occasionally a persons with an otherwise normal integument. Congenital patchy canities is less rare, and may exhibit a strong hereditary tendency The lock f wh te hair is often placed conspicuously on the brown poliosis circumscripta (p. 554)

Acquired Canities may develop rapidly o slowly Canities senilis is the ordinary senile type canities premature is the type which has its onset early Premature grayness manifests itself early with a few gray hairs in childhood, a sprinkling of them during adolescence, and complete grayness by the age of from 25 to 30 years. This is often a familial trait and appears sometimes as a simple dominant character

Graying may be symptomatic. It occurs in endocrine disturbances, particularly thyroid troubles. It is typical for regrowth of hair in alopecia areata to be white at first, but as a rule normal pigmentation is eventually regained. Rats on a diet low in vitamin B filtrate factor develop symmetric patterns of graying an anti gray hair factor p amino-benzoic acid (Sieve Sc 94 257 1941) exists in liver and yeast. The rat anti-gray hair factor failed to help human beings (Bernhauer ADS 49: 132, 1944; Brandaleon et al. AmJMSc 208 315, 1944) and calcium pantothenate was without value in restoring hair color in the experience of Kerlan and Herwick (J 123: 391 1943) Nutritional deficiency in human beings productive of depigmentation of skin and hair has been described in children in Malaya (Nicholls: Lancet 2 201 1916) and in Af ica (Hughes BMJ 2 84, 1946)

Whiteness of hair is due to fa lure of pigment formation in the follicle before cornification takes place Blanching must be a slow process, although the topic of sudden blanching is perennially of interest, however dubious (QMN: J L.I: 161 1913) Dopa positive cells are absent from the region of the follicles. No treatment is necessary The use of hair dyes, which may contain silver nitrate, pyrogallic acid, paraphenylendiamine is frequently injurious (see Redgrove and Foan: Hair Dyes and Hair Dyeing Heineman 1930)

**Ring Hair.**—Ri glike grayness of the hair is a peculiar disorder in which many or all of the hairs of the mustache or scalp exhibit rings of white alternating with rings of pigment Aside from the pigmentary changes, the filaments are apparently normal. The condition is probably analogous t transverse bands of nail (q.v.), representing lternate states of good and poor nutrition of the growth zones of the follicles.

## ALOPECIA

**Alopecia (Baldness)** may be due to any of a number of causes. It may be partial or complete *It may be patchy or universal. It may be*

diffuse, affecting only some hairs of the region, or complete, affecting all in that place. Congenital and acquired types are recognized.

**Symptomatic Alopecia** may be classed as follows

| Cicatricial | Noncicatricial |
|---|---|
| Burns, scald, x-ray avulsion | Mechanical, including friction and trauma, occipital alopecia of infants |
| Favus, kerion, rare types of tinea | Infectious dermatitis, folliculitis, tinea |
| Necrotizing infections | Atrophy of the hair avitaminotic |
| Morphea-like carcinoma | Alopecia areata, local or universal |
| Morphea | Trichotillomania |
| Miliary cicatricial alopecia | Depilation, roentgen or thallium |
| Folliculitis cheloidalis | Alopecia following severe illness |
| Lupus erythematosus | Secondary syphilis, leprosy tuberculosis |
| Pseudopelade | Endocrine disturbance, menopause, melancholia |
| Hemiatrophy or morphea | Premature and senile alopecia |
| Alopecia indurata atrophica | |

These types are almost self-explanatory In cicatricial alopecia destruction of the follicle is the underlying pathologic change. Burns and scalds, roentgen damage, morphea, lupus erythematosus, syphilis, gangrenous herpes zoster lupoid sycosis, folliculitis cheloidalis, favus, kerion, and other scarring diseases receive attention elsewhere.

**Cicatricial Alopecias** include, among the entities listed in the preceding paragraph, dermatoses which do not cause much diagnostic confusion and others which do Laymon and Murphy (JInvD 8 99 1947) clarified particularly the latter including clinical and histologic distinctions between pseudopelade, folliculitis decalvans, lupus erythematosus, and ulerythema sycosiforme They quoted Brocq et al. (AnndeD 6 1 97 209 1905) who in a detailed study classed 3 varieties (1) true pseudopelade characterized by slowly progressive baldness with an insidious onset, without inflammation or pustular folliculitis but with progressive atrophy and with hairs which on removal show a swollen, glassy root lacking demonstrable fungi (2) Quinquaud s type of epilating folliculitis and acne decalvans of Lailler which differ from pseudopelade by the presence of perifollicular suppuration and (3) lupoid sycosis, wherein follicular and perifollicular inflammation is so severe that pustular masses form, the tissues are infiltrated, the expansion of the involved region is eccentric, and keloidal changes occur in the central regions. Laymon and Murphy reviewed and investigated the histologic changes in these conditions

Pseudopelade is a chronic, scarring disease of the scalp insidious in onset, lacking visible signs of inflammation throughout its course but otherwise somewhat simulating lupus erythematosus. The multiple lesions are from 0.5 to 2 cm. in diameter with whitish, slightly depressed, atrophic centers, and sharp margins. The bald patches enlarged by gradual peripheral extension, and the disease is slowly and intermittently progressive. The cause is unknown. Alopecia is permanent. The disease evolves over period of decades. Tonics, particularly arsenic and cod liver oil, are said to be serviceable.

Folliculitis Decalvans is a rare, follicular inflammatory process which eventually leads to circumscribed patches f hairless scar By progressive involvement of neighboring follicles the plaques gradually increase in size to form round or oval asymptomatic lesions of from 0.5 to 2 or 3 cm in diameter The inflammatory pustules are located at the border As active lesions involute, superficial crusts remain, which, on healing with the loss of the involved hair leave tiny red pots which gradually fade. The central region is the oldest and appears as a smooth, shiny bald scar without traces of former follicular orifices. The cause is unknown. The condition is rebellious to therapeutic effort.

Lupus Erythematosus of the scalp begins with small, wine-red, nondiagnostic-able flecks around the follicles. These gradually enlarge and coalesce in irregular plaques.




Figs. 980 and 981.—Folliculitis decalvans.



Fig. 982.—Brocq's pseudopelade. (Dr O. G. Costa.)



Fig 983



Fig. 984

Fig. 983.—Syphilitic folliculitis causing alopecia. (Hazen *Syphilis* Mosby Co.)
Fig. 984.—Cicatricial alopecia due to lupus erythematosus.

While such lesions may remain superficial and erythematous, they are more likely to become slightly depressed, showing central atrophy and pallor and peripheral redness and activity. Scaling is similar to that of discoid lupus erythematosus in other locations, and conical plugs usually remain in the dilated, atrophic follicles. Telangiectases are present both at the borders and in the centers of the plaques.

ULERYTHEMA SYCOSIFORME begins almost exclusively on the face anterior to the ear. It is usually unilateral. It is extremely rare and occurs on the scalp only by extension. Inflammation and infiltration are highly accentuated, the early lesions being large perifollicular pustules which tend to coalesce. The underlying skin is red, thick, and frequently covered with crusts and scales. Extension is centrifugal. Centrally there are complete atrophy of the pilosebaceous system and keloidlike scarring.

MILIARY CICATRICIAL ALOPECIA occurs in old, seborrheic scalps, particularly in women and leads to the production of multitudes of tiny scars scattered irregularly about the scalp. It involves the vertex as a rule. It is distinguished from sycosis, from pseudopelade, and, with considerable difficulty we believe, from neurotic excoriation. Breaking the hair abets this disorder.

ALOPECIA INDURATA ATROPHICA is a sclerosing form of scalp disease affecting the vertex, particularly of women. It is often familial. It causes cohesion of the connective tissue with the underlying aponeurosis so that a hidebound condition of the scalp results, along with diffuse baldness of variable degree, even total. The cause is unknown, and treatment is ineffectual. It sometimes accompanies arteriolar sclerosis with hypertension. Estrogen therapy deserves trial.

## Noncicatricial Alopecias to be considered are as follows

MECHANICAL ALOPECIA implies simply the breaking off of the hairs through manipulation, such as the friction of the infant too young to sit, against its bed. Hair is more fragile in some persons than in others. Overzealous medication and washing can cause alopecia. Alopecia of men's legs appeals to us as being of frictional origin (Tommasi: BJD 52: 1, 1940).

TRICHOTILLOMANIA is a neurotic habit of pulling out hair.

EMOTIONAL SHOCK is said to have been followed by total defluvium, which was temporary. This is doubtless a form of alopecia areata.

TOXIC OR FEBRILE ALOPECIA commonly accompanies typhoid fever, influenza, pneumonia, septicemia, and other severe sicknesses. The hair is considerably thinned, sometimes lost. Prognosis is good after recovery from the primary illness.

CACHECTIC ALOPECIA is a frequent condition in tuberculosis, and may occur in diabetes mellitus, rickets, and other wasting disorders. The hair loss is qualitative as well as quantitative, the few new hairs in the regrowth usually being finer and more lanugo-like than the old, and complete recovery seldom if ever takes place.

ENDOCRINE DISTURBANCES associated with loss of hair are varied and complex. In pituitary emaciation there is loss of hair from the pubic and axillary regions, the eyebrows, the lashes and the scalp. Hypothyroid baldness begins along the margin of the scalp oftenest about the temporal eminences, less frequently at the occiput, rarely extending to the vertex unless in a terminal complete involvement. Melanoderma is often part of the picture of hypothyroidism. Hirsutes thinning and coarsening of the scalp hair, loss of weight and of appetite, and increase in general pigmentation are commonly seen. Simmonds' disease (Escamilla and Lisser: JClEndocr 2: 65, 1942) and progeria (Moehlig: J 132: 640, 1946) are associated with gray and scanty hair.

SEBORRHEA.—Of the chronic inflammatory disorders of the scalp which are imagined to give rise to hair atrophy and hair loss seborrhea and seborrheic dermatitis are usually inculpated. Alopecia pityrodes first involves the temporal and frontal regions, and is accompanied by more or less furfuraceous desquamation. Regression of the hair line in lateral V's progresses, and a circular patch of thinning enlarges over the crown. The denuded areas, with feeble lanugo where hair once thrived, slowly approach one another leaving a forelock in the middle of the frontal region. This goes too in time and a fringe alone surround a glistening pate.

ALOPECIA SENILIS, associated with old age, is characterized by symmetric thinning of the hair on the vertex and in the temporal regions although occasionally nearly the entire calvarium is involved. Its appearance and course do not differ from seborrheic or premature forms excepting in age of onset (Buttner: ADS 44: 201, 1941. Templeton: ib., p. 31,, inheritance).

PREMATURE ALOPECIA that form of acquired baldness which occurs without determinable cause in relatively youthful individuals. Premature alopecia appears to indicate masculinity because children, females, and eunuchs do not exhibit it (Hamilton:

AmJAnat 71: 451, 1942) Baldness occurs more frequently in persons with relatively heavy growth of body hair (Harris BJD 59: 300, 1947) Hoping to feminize an experimentally inclined and balding physician friend of ours and so to alter the course of his alopecia, we once administered stilbestrol, the effects of which were, mildly stating the facts, unsatisfactory Calcification of the skull was the explanation not facetiously given by Hoelzel (J 119: 968, 1942) and fluorine was incriminated by Spira (JHyg 44: 276 1946) whose logic was not Aristotelian. Since masculine alopecia is of un-



Fig. 985.



Fig. 986.



Fig 987

Fig 985 —Trichostasis spinulosa. (Dr James H. Mitchell.)
Fig. 986.—Knotted hairs (Dr F Ronchese.)
Fig. 987 —Ring hairs. (Dr Fred Weidman.)



Fig. 988



Fig. 989



Fig 990

Figs. 988 and 989 —Alopecia due to traction (alopecia liminaris frontalis) (Costa and Junqueira AIbS 48 527 1943.)

Fig 990.—Poliosis circumscripta, white forelock.

known etiology is compatible with an existence successful in every respect, and is irremediable we advise the sufferers who seek our aid to accommodate their ego to their destiny

ALOPECIA FROM LOCAL CAUSES is due to destruction of follicles by ulceration and formation of scar tissue. In addition to various injuries, furunculosis, ulcerating syphilids, and kerions occasionally give rise to patchy baldness. Lupus erythematosus may involve areas of considerable extent on the scalp, and the ensuing hair loss is permanent. In morphea, also, baldness is a characteristic feature of the affected areas. In ordinary tinea capitis, the hair loss is due to destruction and fracture of the hair shafts, the bulbs being unaffected; consequently such alopecia is only temporary

Twisted Hair (Pili Torti of Galewski and Ronchese) is a rare anomaly characterized by twisting of the hairs. In Ronchese's cases in a brother and sister the affection dated from birth. It was accompanied by dryness and brittleness of the shaft, which resulted in alopecia over the occiput due to the habit of sleeping on the back. The case of Siskind (ADS 56: 640 1947) followed scarlatina at age 10 and improved markedly on vitamin A, 200,000 units per day

Knotting of the Hair is commonplace.

Congenital Hypotrichosis.—Partial or even complete deficiency or absence of hair may be a manifestation of congenital ectodermal defect (q.v.) Dominant inheritance with similarities to pachyonychia was noted in cases of Beally and Livingood (ADS 47: 455 1943)

Circumscribed Hypotrichosis of Men s Legs.—In many men, there occurs a bald area on the legs. Efforts have been made to link this with baldness of the scalp, but explanations have not been satisfactory (Konshaw and Chase ADS 40 416, 1939) See mechanical alopecia.

Alopecia Liminaris Frontalis (Traumatic Marginal Alopecia).—Persons with kinky hair whose coiffure involves traction lose hair about the margins of the scalp (Spencer: ADS 44 1062 1941 Costa and Junqueira: ib. 48 337 1943) If the hair is more than normally fragile as a result of endocrine or nutritional disorder the mechanical agency is more influential.

**Alopecia Areata.**—Bald patches develop suddenly on otherwise apparently normal skin They range greatly in size, being rounded areas which sometimes overlap The scalp is the site of predilection, although the eyebrows, bearded region, pubes, axillae, and any part of the body may be involved. Sometimes the first intimation of the disorder is the sudden detachment of a large bunch of hair Occasionally the outfall is gradual, several days being required for the development of appreciable baldness. The spots enlarge peripherally for a few days or weeks. In the universal cases, which fortunately are rare, all hairy regions are affected, and the skin may become absolutely bare. At the margins of spreading lesions, loose shafts may exhibit atrophic changes near the mouths of the follicles, the altered shape of their proximal ends more or less justifying the title, exclamation point hairs These can be extracted easily and painlessly during the spreading stage of the attack. The skin of the bald spots is normal in consistency and is not inflamed Regrowth takes place slowly in the ordinary cases. The first crop of hair is usually thin, white, and lanugo-like and is likely to fall out after the shafts have attained a length of 1 cm. or so. The second or third regrowth usually persists. Regrowth is less likely in older patients and when large areas are involved, and loss of hair may be permanent See Baukus (NYSJM 36 1929 1936) Peterkin (MP&Circ 201 520 1939)

The cause is not known The disease affects the sexes with equal frequency and is commonest between the second and fourth decades of life. Typical lesions sometimes follow traumatic neuritis. Abscessed teeth and hyperplastic or infected tonsils are often associated. Anxiety nervous shock, fatigue, and worry are certainly connected with causation in some



Fig. 991.—Alopecia areata.



Fig. 992.—Alopecia areata.





Fig. 993.—Alopecia areata involving beard.



Fig. 994.



Fig. 995.

Fig. 994.—Alopecia [illegible] lis not [illegible] hair on entire body. (Dr. H. N. Cole.)
Fig. 995.—Trichotillomania.

manner Time after time we see the onset of alopecia areata coincidental with such influences as death in the family business failure, divorce or working the night shift.

Many patients promptly regrow their hair and feel much better when given thyroid extract. Arsenic, iron, cod liver oil, diuretics, cathartics, hexamethylenamine, and other medicines have been given empirically Pure phenol, lightly swabbed over the area then wiped off with alcohol, is of value (Bechet: ADS 44 512, 1941) Rubefaction with ultraviolet light justifies more or less enthusiasm (Peterkin MP&Circ 201: 520, 1939) Rest and relief from anxiety and fatigue are essential. Focal infections should receive attention (Grace ADS 45 349, 1942) Foreign protein therapy may be undertaken. No proof of endocrine etiology could be discovered in universal cases by Waisman and Kepler (J 116: 2004 1941) Pituitary extracts may encourage regrowth (Thorner Endocr 26 433, 1940) Androgenic substances deserve a try (Stalder abs ADS 54 217 1946)

**Vogt-Koyanagi Syndrome.**—Uveitis, sometimes with retinal detachment dysacousia, vitiligo poliosis and alopecia are collectively seen occasionally in one patient, and such cases constitute a fairly well-defined group (Givner AOphth 30: 231 1943; Hague: ib 31: 520, 1944) In the case of Behrman et al. (ADS 67 233, 1946) the woman's spinal fluid contained 00 lymphocytes per cu. mm. and increased protein, but the search for a virus cause was inconclusive.

## SYCOSIS VULGARIS

Sycosis vulgaris is chronic folliculitis or perifolliculitis especially of the bearded region, associated with the presence of staphylococci. The disease is usually limited to the bearded region, but the scalp may be involved by extension. The forearms and other hairy areas may rarely be affected. The essential lesion is a deeply seated or superficial papule or pustule, pierced by a hair After a lesion has persisted for several days its hair can be extracted easily usually along with the root-sheath. In old, pustular lesions, hairs are quite loose. The malady often begins on the upper lip accompanying or following nasal infection, and from this locality it gradually spreads to other parts of the face. Ultimately it may involve not only the mustache and bearded regions, but also the eyebrows, lid margins, scalp axillae, and pubes. Destruction of hair and subsequent cicatrization are ordinarily comparatively slight, but alopecia may be extensive and scarring a prominent feature. The inflammatory process is not so acute as in tinea barbae and, boggy kerion-like swellings are absent. The clinical picture remains that of pustular folliculitis. The eruption may be scattered or limited to one or two small areas, and such areas may expand and coalesce or it may involve the entire bearded region. The course of the disease is tediously and rebelliously chronic While a few lesions may undergo spontaneous involution, new crops of papules are constantly springing up. Blepharitis, typically marginal, along with more or less severe conjunctivitis, is the usual accompaniment of severe sycosis.

The patient is generally of poor economic and social condition in the United States, but sufferers from the disease in Great Britain are often of well to-do classes Sycosis vulgaris is thought to be due to strains of *Staphylococcus pyogenes* Lowered resistance is a contributory factor whatever the term may mean perhaps avitaminosis is concerned. Pus, microorganisms, and serum are found in the mouths of the follicles, the epithelial walls of which are edematous and permeated with leucocytes

As in all inflammatory processes, both the soil and the parasite must be taken into consideration. The problem seems to be one of altering the flora perhaps this can be attacked by way of altering the soil, but staphylococcic vaccines are in general ineffectual. Staphylococcic toxoid was tested by Forman (YBD 1937 p 386) in 21 cases, in which its use was followed by 2-fold to 24-fold increase in antitoxic titer of the blood, but not by benefit.

Focal infection must be attacked with energy Oral foci include dead teeth dental root abscesses, pyorrhea, broken and decayed teeth and infected tonsils. The prostate, bladder or urinary tract may harbor significant infection.



Fig 196 —Sycosis vulgaris.



Fig. 197 —Perforating folliculitis.

The patient should be supplied with a good pair of epilating forceps and instructed in the removal of the diseased hairs Each day the involved area should be poulticed with hot towels, carefully inspected, and all infected hairs epilated. This is followed by an antiseptic ointment such as 2 per cent ammoniated mercury or 3 per cent Vioform. Peck and Chargin (ADS 29 456 1934) recommended

| | | |
|---|---|---|
| ℞ | Oxyquinoline sulfate | 0.25 |
| | Benzoyl peroxide | 5.0 |
| | Eucalyptol | 0.5 |
| | Oil of thyme | 0.5 |
| | Petrolatum | to 50.0 |

The addition of 1 to 2 per cent sulfur increased the efficiency of the ointment. Vitamins, especially cod liver oil riboflavin, and nicotinic acid are helpful, and alcohol must be interdicted (Whitehead PaMJ 42 1193 1939) Sulfonamides may be recommended especially when they help to clear the urinary tract. Penicillin locally by compresses of 250 units per c.c. (Alderson ADS 55 573, 1947) or in an ointment vehicle (Russell: BJD 59: 294 1047) is likely to improve matters temporarily Roentgen therapy is valuable Shielding and technic must be meticulous to prevent ocular damage or unwanted hair loss. In dealing with refractory cases, after conservative therapy has failed the advisability of effecting permanent alopecia by x ray may be considered.

## FOLLICULITIS

**Folliculitis Cheloidalis (Dermatitis Papillaris Capillitii)** is an exceedingly chronic inflammatory process, involving the skin of the nucha. It is characterized by folliculitis productive of nodular lesions of sycosiform and keloidal aspect.

The disease begins with the formation of acuminate, pinhead size nodules at the border of the hair. The little tumors are reddish and firm. They tend sometimes to coalesce, forming rough keloidal plaques. They may enlarge to cherry size. On section they are hard and gritty. When punctured they bleed freely. Pustules may spring up between the lesions, or the entire group may become undermined and boggy with circumscribed subcutaneous abscesses. Tufts of twisted, deformed, and broken hairs project at many points through the nodules. The cause is not known, but a combined acneic microbic and traumatic origin seems probable.

The lesions do not tend to regress spontaneously and they are rebellious to treatment other than with low fat diet, thyroid, and x rays. Filtered radiation should be used and treatment ought to be undertaken early before much keloid formation has taken place. In late stages it is generally necessary to push irradiation to the point of permanent alopecia. Excision of grossly deformed follicles, cysts, and nodules may be indicated.



Fig. [illegible]



Fig. [illegible]

Fig. [illegible].—Acne cheloidalis (dermatitis papillaris capillitii)
Fig. [illegible].—Perifolliculitis capitis abscedens et suffodiens.

**Perifolliculitis Abscedens et Suffodiens.**—This rare disease characterized by multiple abscesses of the scalp with undermining, granulomatous cellulitis is a severe affection. Many large and small nodules suppurate and intercommunicate by burrowing. The lesions are hard to control by treatment and on healing leave irregular flat scarred, bald spots, similar to those following folliculitis decalvans. The active nodules present the *structure of granulomas with features suggestive of a tuberculous process.* Cutaneous myiasis can produce a similar picture although, of course, larvae are present. The 5 patients of Arbeck (abs YBD 1943, p. 181) all of whom were by occupation exposed to atmospheric influences, were unresponsive to therapeutic effort until the nodules were excised, after which the wounds promptly healed. Fever therapy and x-ray epilation have been recommended (Cannon ADS 49: 67 1944). We agree with Brunsting's views regarding the case associated with hidrosadenitis of crotch and axillae of Omens et al. (ADS 48 226, 1943) that the process is an acneiform affection. We attack our cases, rare as they are, with low fat diet, thyroid, and elimination of focal infection. Sulfathiazole helped the patient of Barney (ADS 44: 130, 1941), and penicillin intramuscularly the patient of Cornbleet and Kagen (ADS 53; 543 1946).

**Perforating Folliculitis of the Nose.**—A follicular abscess of a hair within the nostril may perforate the skin externally. The bulbous base of the vibrissa is presented within a small pustule on the external surface of the nose. Following extraction of this hair such lesions promptly heal (Rees ADS 44 969 1941; 45: 235 1942).

## TRICHOSTASIS SPINULOSA (PINSELHAAR BUNDELHAAR LANUGO COMEDONES)

This peculiar disorder affects hair follicles of the shoulders, back, and sides of the thorax. The follicles contain blackish, elevated horny spinous plugs, which fill the dilated orifices but can easily be removed. These keratotic plugs contain bundles of lanugo hair, which protrude beyond the niveau and can readily be palpated. The nape of the neck and the back are the common sites, but the peculiarity has been observed in many regions. The deformity seems to be a congenital one, and treatment is only palliative Recourse may be had to salicylated oils or ointments locally and thyroid and vitamin A by mouth. See Mitchell (ADS 11 80 1925) and Feinburg (ib. 27: 274 1933)

# DISORDERS AFFECTING THE NAILS

## NAIL GROWTH AND MANIFESTATIONS OF ABNORMALITY

Nails are analogous with hairs in their embryology structure, and physiology Picture a hair which grows from a point and is set perpendicularly in the skin, transformed into a structure which grows from a transverse line and is set so obliquely that it extends as a practically horizontal plate. As the hair grows, so grows the nail, with the geometric difference that the hair is the extension of a point that is, a line; and the nail is the extension of a line, that is, a surface. Produced as the nail is by a line, it extrudes like the roll of a player piano. What alters its source must register a corresponding mark on the plate.

The growth zone of the nail is a line curved convex distally It is a curve parallel with the distal margin of the lunula. Beau's lines are transverse bands due to temporary damage of the entire growing zone, and they parallel this curve. A band across the nail curved concave distally is due to trauma, usually from manicuring A band concave distally could not result from a systemic influence.

The nail bed grows outward with the nail plate, which to some extent *depends on it for nutrition, for the plate becomes cloudy* discolored and distorted when separated from the bed. If subungual hemorrhage occurs, the stain grows out with the nail If a mark is made on the nail bed after surgical removal of the plate, the mark grows out ahead of the nail instead of becoming covered by it While this is true, the important clinical fact is that the nail behaves as if it grew from a line about 8 mm. proximal to the distal edge of the lunula. It slips distally over the dorsum of the phalanx just as a hair pushes outward past the walls of its follicles. Nails grow at the rate of about 1 mm. per week. Given understanding of these concepts, interpretation of nail plate manifestations is simple.

**Systemic Disease,** which say, for one week damages the nutrition of the entire growing zone of all 20 nails, will result in the appearance on each nail plate of a transverse line convex distally visible as soon as the nail has grown out far enough to be seen beyond the proximal nail fold and every nail will be similarly affected. The width of the line must be about 1 mm malnutrition having lasted a week by hypothesis. Looking at the series of Beau's lines, as such transverse bands are called, one readily estimates—on the basis of 1 mm per week—how long ago it was when the damage occurred

**Local Dermatitis,** if it alters nail nutrition by causing inflammation of the terminal phalanx of the digit must similarly leave its mark on that nail. Contact dermatitis and aerodermatitis so mark the nails.

**Evanescent Disorders** damaging the growing zone at scattered points over a *period of time register themselves on the nail plate* as a scattering

of thin spots, pits. Following a shower of miliary injuries, pits may range across the plate in an arc. The period during which this occurred is gauged by the length of nail plate involved.

**Transverse Bands of All Nails** signify temporary damage of all nails, which implies systemic disturbance.

**Transverse Bands of Isolated Nails** signify temporary damage of the involved nails as a result of local disturbances, which might of course be the local accidents of systemic disease.



Fig. 1000.



Fig. 1001.

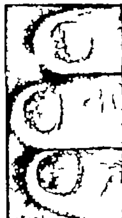


Fig. 1002.

Fig. 1000.—Transverse striae due to acute pellagra 6 weeks previously. (Brownson, BMJ 2: 672, 1918.)
Fig. 1001.—Longitudinal striae due to use of fluoroscope.
Fig. 1002.—Injury of nails by photographers' chemicals.



Fig. 1003.



Fig. 1004.



Fig. 1005.

Figs. 1003 and 1004.—Nail damage from episodes of eczematous dermatitis.
Fig. 1005.—Spoon nail. (Dr. H. C. V [illegible].)



Fig. 1006.



Fig. 1007.

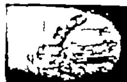


Fig. 1008.

Fig. 1006.—Periungual fibroma. (Dr. O. G. Costa.)
Figs. 1007 and 1008.—Verruca of nail fold.

**Shedding of the Nails** is the maximum of defect of the Beau s line sort. Regrowth usually occurs. Shedding, as distinguished from avulsion and onycholysis, simply means that the nutritional disturbance was violent and fairly enduring. Shedding of the nails is a common sequel of scarlet fever and it may occur in the course of other systemic maladies, such as alopecia areata, typhoid fever and exfoliative dermatitis.

**Permanent Alteration** of the growing zone occurs, produced by roentgen or arsenical damage or by the presence of a nevus or a cicatrix. The result is that a fraction of the growing zone is permanently different from the remainder The nail substance growing forth from it is different the nail plate must register a longitudinal stripe.

**Longitudinal Lines** signify enduring or perhaps permanent alteration of the growth zone of the affected nails. Congenital defect is a common cause. When the ten fingernails show longitudinal lines, and the toenails do not, the cause is very likely to be x ray injury such as affects the hands of physicians using fluoroscopes carelessly When all twenty nails show such lines, the cause is very likely to be arsenic.

## GENERALITIES ON ETIOLOGY PROGNOSIS, AND TREATMENT OF DISEASES OF THE NAILS

**Outline of Nail Disease.**—Nails are influenced by

MALFORMATION as in congenital ectodermal defect.

NEOPLASIA, such as melanoma, carcinoma, exostoses.

TRAUMATIC, PHYSICAL, MECHANICAL, AND CHEMICAL INJURIES of various sorts, which may loosen the plate from its bed, as a blister loosens the epidermis from the dermis below A bruise may cause hemorrhage beneath the plate.

Hemorrhage manifests itself as a bluish purple petechia variable in its effect on the growth of the plate in accordance with its location with regard to the growing zone.

Physical factors of the environment affect the nails, such as low humidity in winter which leads to brittleness of the nails. Nails are loosened from their beds by exposure to excessively hot water—people differ in their vulnerability to this kind of trouble—and by exposure to alkali or acid, and by the habitual trauma of occupationally or nervously picking at something Mechanical distortion of the foot by tight and ill fitting shoes is the commonplace cause of forcing soft tissues into the path of the growing nail so that ingrowing nail results.

METABOLIC ALTERATION of the bodily economy In avitaminosis nails suffer along with other epidermal structures. In hyperthyroidism, they are likely to be thin and fragile. In the Plummer Vinson syndrome koilonychia is a typical symptom. Leuconychia, white spots within the nail, is characterized by loss of translucency of the nail plate because of incomplete degeneration of the horny cells. They contain droplets of a substance of which conversion into keratohyalin has not quite succeeded. The spot is white, then, for the same optical reason that milk is white Such whiteness occurs in scattered spots, gift spots, as they are called; sometimes it occurs as an affection involving the entire plate of all the nails as such, leuconychia totalis comprises a curious form of ectodermal anomaly which shows decided hereditary tendencies.

INFLAMMATORY ALTERATION WITH LOCAL ACCIDENTS to the nails, as in syphilis, leprosy lichen planus, psoriasis, pemphigus, scleroderma, dermatitis venenata, pustular acrodermatitis, infectious eczematoid dermatitis, keratoderma gonorrheica, and granuloma pyogenicum. These influence the nail through their incidental alteration of local tissues. Diseases of the

nails and dermatoses of the digits are really separate subjects, for nail diseases proper are those which are peculiar to the nail itself, while digital diseases comprise almost the totality of dermatology Thus parasitic inflammatory affections fall into 2 classes:

PARASITISM PRIMARILY OF ADJACENT SOFT TISSUES, such as infection with the virus of verruca vulgaris with staphylococci, streptococci, or bacilli, such as that of anthrax, with spirochetes, such as that of syphilis with fungi, such as those of tinea, moniliasis, and sporotrichosis and with animals, such as *Sarcopsylla penetrans*.



Fig. 1009.—Streptococcic paronychia, same bacterium in dermatitis and dental abscess.

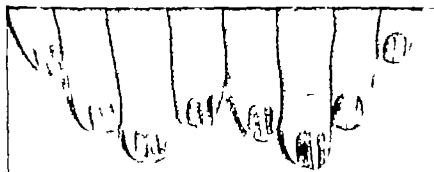


Fig. 1010.—Onycholysis and subungual hyperkeratosis caused by nail lacquer adhesive. (Winston and Sutton JAMA 49 871, 1942.)



Fig. 1011.—Leuconychia totalis. (Stubenbord and Stubenbord ADS 32: 761, 1935.)

PARASITISM OF THE NAIL PLATE. Nail substance is chemically the same, for practical purposes, as the stratum corneum It is a suitable culture medium for many of the fungi imperfecti, which grow into it from its free margin. If the proximad progress of the growth of the fungi exceeds the rate of distad growth of the nail plate, inevitably the nail becomes more

and more extensively involved and damaged, until there may remain only a crusted, flaky mass of distorted material extending actually underneath the proximal fold and supplanting the entirety of the nail plate. The infected nail is an important focus of mycotic infection. See onychomycosis and mycotic paronychia.

NEUROTIC HABITS.—Onychophagia and onychotillomania and perhaps the attrition and polishing induced by scratching may be included here.

COMBINATIONS OF FACTORS.—Nails may be malformed, malnourished, traumatized, scarred, infected, and neglected, to variable degrees by such influences in various combinations.

**Prognosis.**—A nail capable of growing is able to replace itself in about 4 months. The outlook for ultimate replacement therefore depends on whether the growth zone is permanently altered, and whether the locally damaging influences can be removed. Damage to the plate distal to the growth zone is temporary for the structures are replaced. Traumatic separation of the plate from its bed, accidental or purposeful, heals in due time with a noteworthy lack of distortion. Malformations are irremediable excepting by the radical correctional revisions of plastic surgery. But systemic diseases can often be treated with success. Mechanical troubles are usually easy to correct. Local inflammation requires its individual interpretation and prognostic assay. Melanoma of the nail bed is highly malignant and requires amputation.

**Treatment.**—In general, one attacks the underlying cause if possible. Nutritional deficiencies, hypothyroidism, and infections, such as syphilis, are responsive. Onychomycosis and mycotic paronychia have been discussed. Mechanical lesions, such as those due to manicuring are easily altered. Local injuries, inflammatory manifestations, and inflammatory diseases must be met in accordance with dermatologic principles just as one would if the trouble were located elsewhere. One does not need to hesitate to perforate the nail plate to let pus out from beneath it. After injecting Novocain deep into each side of the proximal phalanx for obtaining local anesthesia, one may freely cut across a nail plate and tear off the distal portion; regrowth and healing take place in due time. One may destroy the epithelium of the nail bed by the superficial blistering application of the cautery after removing the plate distal to the growing zone; and healing and regrowth under simple greasy dressings take place almost painlessly and with little permanent distortion. Severe verrucous paronychia and rare subungual verrucae are thus treated effectually. It is necessary not to mistake pyogenic paronychia for ingrowing nail and so to perform one of the various plastic operations on soft tissues designed to pull them away from the direction of nail growth. Neoplasia demands surgery rather than dermatology. Finger pulp infections, felons, likewise we leave to surgery along with other infections of the hand. A furuncle in a digital hair follicle is *not* correctly treated by extracting the hair; this procedure is likely to result in a subcutaneous abscess.

## SPECIFIC DISEASES OF THE NAILS

**Psoriasis** affects the nails. When the nails alone are affected, the changes are the same as when the nail involvement is only a part of the patient's psoriasis. There occur detachment of the plate, alterations of the plate likely to end in partial destruction of the nail, changes in color, shortening of the nail, and pitting (White: UCalRev 42: 69, 1939.)

**Pigmentation of the Nails.**—Permanganate of potassium, commonly used for soaks in dermatology, stains the nails mahogany brown. Chrysarobin stains the nails

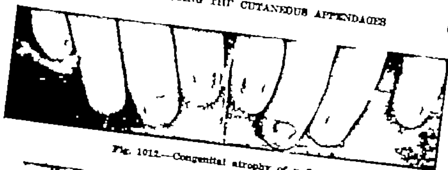


Fig. 1012.—Congenital atrophy of nails.

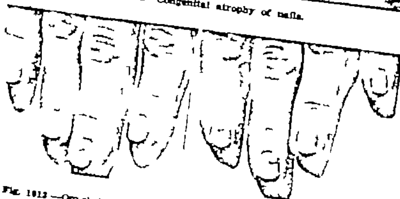


Fig. 1013.—Onycholysis, cause undetermined. (Dr. John Shahan.)

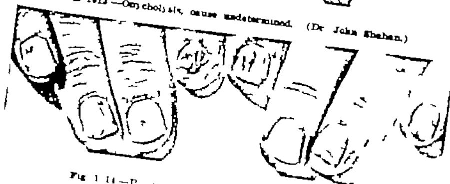


Fig. 1014.—P[illegible] of [illegible] (Dr. D. E. H. [illegible]land.)

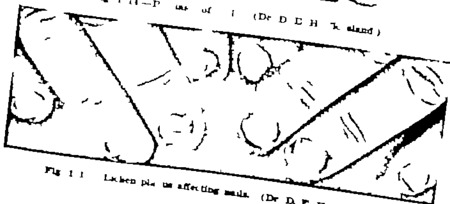


Fig. 1015.—Lichen planus affecting nails. (Dr. D. E. H. Cleveland.)

yellow brown. Dystrophic, onychogrypotic and mycotic nails are variously discolored, being dark, blackish, brownish, greenish, or gray. Pigmented bands occur as longitudinal striations when due to a pigmentary nevus at the growing zone. Roentgen dermatitis and arsenical keratosis lead to the production of discolored longitudinal striae. Subungual hemorrhage discolors the nail.

**Onycholysis** is a term applied to loosening of the nail from its bed not primarily as a result for growth zone failure. When not traumatic, or due to hot water or alkali the condition is usually symptomatic of nail matrix disturbance such as may occur in psoriasis, contact dermatitis, or syphilis. Trauma, such as that occasioned by short shoes and athletic enterprise, may blister off a toenail, especially if it is trimmed long.

**Eggshell Nail** is a peculiar disorder characterized by upturning of the free border with increased translucence of the entire plate. It is seen in avitaminosis A.

**Onychogryposis** is a term applied to extreme cases in which affected nails become greatly elongated and clawlike.

**Onychauxis** is hypertrophic overgrowth of the nail plate. It may be congenital or acquired, idiopathic or symptomatic. Included under this head are the nail changes in acromegaly and the clubbed fingers of phthisis and other chronic pulmonary affections.

**Onychorrhexis (Brittleness)** of the nails may be congenital or acqured. There may be coincident longitudinal furrowing, and there is usually more or less thinning of the nail plate. Low humidity nail polish and polish removers, frequent washing with hot water and alkaline soaps, and hypovitaminosis A are causative factors.

**Onychophagia**, or biting of the nails, is a neurotic habit.

**Usure des Ongles** is the French designation for the attrition, terminal curvature, and polishing of the nails which occurs as a symptom of widespread pruritus and the scratching so occasioned.

**Malformation.**—Anonychia is total absence of nails, a rare congenital anomaly Displacement or heterotopy of the nails has been seen. Gigantism of a nail may be seen in Recklinghausen's disease of a digit. Pachyonychia is an interesting malformation manifested as wedge-shaped thickening of the nail plates, so that the distal edges may be several millimeters thick. It is often associated with hyperkeratosis of the palms and soles.

**Median Canaliform Dystrophy** is manifested by a curious lo gitudinal streak i which the nail is folded in a slender cylinder (Heller: DZtschr 51: 416, 1928) Extending from the root to the free edge, where the nail becomes fissured the anomalous condition, a rarity, has something to do with parakeratosis (Robinson and Weidman: ADS 57 328, 1948) The streak is pigmented, and several of the few reported cases have affected the thumbnails.

**Neoplasia.**—See adenoma sebaceum with subungual lesions melanoma, and melanotic whitlow; subungular exostoses; glomus tumor Primary squamous carcinoma of the nail bed is extremely rare.

**Trauma.**—A crushing injury such as the blow of a hammer is likely to cause subungual hemorrhage. At first red the extravasated hemoglobin is transformed as it is in an ordinary bruise, becoming black. If the blood blister occurs within the growing zone, the nail is shed partially or completely and regrowth eventually occurs. Petechiae sometimes occur under the nail in purpura. An injury which cuts through the growing zone and scars it leads to the development of a permanent longitudinal stripe. The analogues of friction blisters of the skin may form under the nails under suitable mechanical conditions. Persons afflicted with congenital ectodermal defect or epi dermolysis bullosa are particularly susceptible. Dissolutions of adherence between nail plate and bed are likely t become infected with pyogenic organisms, as other blisters are. The subungual purulent bleb which results is exceedingly painful until a window is cut in the overlying already separated nail plate to let out the exudate. One should flush the cavity then let soap in a liquid antiseptic such as tincture of Merthiolate.

**Ingrowing Nail.**—*The lateral border or distal edge of the nail may grow into the soft parts.* T ght shoes are the common cause, for they force the soft tissues of the lateral fold, particularly at the end of the great toe into the direction of growth of the nail. To trim the nail by cutting under the fold is an error which makes the disturbance likely to occur Often in so cutting the nail the edge is not quite reached by the cut, and a sharp sp ke at the edge grows forward into the flesh. Such a lesion is exquisitely sensitive to pressure over the spike. Secondary infection is common. Prevention is preferable to treatment: wear shoes of ample spaciousness, and trim the distal edge of the nail transversely so that its lateral margins lie beyond the ends of the lateral nail folds.

In treatment, one may repeatedly shove cotton under the nail at the edge until the nail grows beyond the end of the toe. One may cut away the nail and pull it from the cavity; but recurrence is likely. One may split the nail longitudinally near the lateral fold and excise the fold itself and the proximal growth zone tissue, so that that part of the nail is permanently amputated.

Pterygium is abnormal adhesion to the nail plate on the part of the epidermis overlying the proximal nail fold. The disorder may be congenital, or acquired as a typical manifestation of roentgen dermatitis.

Hangnails are torn filaments of epidermis, lying free distally and attached proximally so as to tear deeper as they are pulled back. One may flatten the filament and secure it with flexible collodion. With a razor blade, one may notch the skin in wedge shape proximal to the hangnail so as to remove the tag and to reform the lesion from a tearing one into a simple wound, to be touched with an antiseptic. Low humidity and defatting agents are the usual causes.

Paronychia is characterized by acute or subacute inflammation of the periungual tissues of one or more of the nails. The process may be peripheral, but sometimes the disease undermines the nail even to the extent of causing it to shed. Streptococci and staphylococci are causative, and focal infection, especially of the teeth is significant in recalcitrant cases. Trauma, foreign bodies, syphilis, and dermatitis of the hands are other possibilities. Cases have been reported due to many agencies, including tuberculosis, blastomycosis, sporotrichosis, leishmaniasis, and fungi. Rockwood (NEngJM 209: 295, 1933) found many kinds of fungi in her cases. All kinds of infections may be inoculated into finger tips, warts as well as cocci having been introduced by dirty manicuring instruments.

When a purulent pocket lies adjacent to the lateral border of the nail beneath the nail fold, provoking local swelling redness, and pain, it is simply a furuncular lesion within the crevice pointing toward the nail. Soak the digit in hot water for few minutes to soften the tissues, then put into the fold the point of a scalpel, the cutting edge away from the nail. Move the point gently back and forth in the nail fold, pressing it deeper until it painlessly opens into the purulent pocket. Hot soaks and tincture of iodine soon complete the cure.

Diffuse paronychia, in contrast with the local abscess described above, is not so easily cured. It is often streptococcic or mycotic in origin, rather than staphylococcic and it may depend on foci of infection, as pustular acrodermatitis does. Elimination of foci, x ray therapy and penicillin by injection are useful therapeutic measures.

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Ingrowing.—*Chapman* BMJ 2 1072, 1924 (scrape central longitudinal zone thin, lift edge from sulcus, keep pledget beneath until spur grows distal [ fold) *Bartlett* J 108 1257 1937 (cut wedge from side of toe [ pull overlapped fold free) *Kirschenmann* AmJSurg 36: 349 1937 (excise lateral third of nail plate, growth zone and skin of fold in one piece) *Nuttall* Lancet 2 100, 1941 (technic of ablation of nail) *Monson* USNMBull 41 1090, 1946 (remove lateral third of nail plate and matrix without removing soft tissue

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# DISORDERS AFFECTING THE SUDORAL GLANDS

## HYPERHIDROSIS AND ANHIDROSIS

**Hyperhidrosis** is the excessive production of sweat. It may be idiopathic or symptomatic, recent in onset or of long duration, generalized or circumscribed, and unilaterally or otherwise systematically distributed. It is a common symptom in disorders such as tuberculosis, malaria, brucellosis, Graves disease, and diabetes. It is provoked by warmth, nausea, pilocarpine, and vasodilators, such as alcohol and aspirin. Anxiety neuroses, and nervous tension cause sweating usually of the volar surfaces and axillae rather than of the glabrous skin. Sweating is generally greatest in the regions normally rich in coil glands.

Hyperhidrosis in rare cases occurs intermittently in exhausting drenching sweats. Disabling attacks preceded by hypothermia occurred in the man described by Hoffman and Pobirs (J 120 445 1942). In the patient of Hines and Barnick (PSMMC 9: 703 1934) it was necessary to replace chlorides to relieve exhaustion and to give atropine and Amytal to reduce central irritability. In 5 extreme cases, Adson et al. (J 106 360 1936) were constrained to perform sympathetic ganglionectomy which relieved the condition. The skin at once became dry and pink, but the glands did not undergo atrophy.

**Localized Hyperhidrosis** is an interesting phenomenon. The areas involved differ greatly in size and distribution. A lateral half of the face or even of the entire body may be affected. Hyperactivity is confined to glands in areas of sympathetic nerve distribution. Gustatory reflexes provoke curious patches of hyperhidrosis in some persons. Local hyperhidrosis can be relieved symptomatically by the use of astringents, underarm deodorants and x ray therapy. The common commercial antiperspirational and deodorant toilet preparations are in general harmless. If one brand proves to be a source of dermatitis venenata, another may not.

**Volar Hyperhidrosis.**—The palms and soles of some persons are continually cool and wet; they sometimes actually drip. This condition is regularly present in anxiety states and psychoneuroses with tension. We saw great numbers of such cases among neuropsychiatric military casualties and tried with diligence and some ingenuity to relieve them but were unsuccessful. Wet hands and feet are vulnerable to pompholyx and recurrent stubborn eczematoid dermatitis of a sort which may be attributed to nerves, if any dermatosis justly may be. The advisability of x ray therapy in doses which damage sweat glands is debatable, but we favor the measure if the physician knows when to stop. Benadryl or barbiturates may diminish the sweating symptomatically. Extreme cases were reviewed by Haxton (BMJ 1: 636, 1943). Some of his cases having been treated by sympathetic section, which afforded prolonged, possibly permanent cures. Usually no cause can be found, he stated, but among known possible causes are irritative lesions of the sympathetic pathways.

**Unilateral Sweating** results from neural lesions which stimulate sympathetic fibers, seen in epidemic encephalitis, lesions and tumors of the brain stem, and unilateral frontal lobe lesions; and sometimes in migraine. Aneurysms, new growths, tabetic crises (band of sweating) and syringomyelia are listed as causative of localized sweating.

**Sweating Sickness** is of historical interest. It occurred in explosive epidemics strange, unexplained and serious in the Middle Ages with erythema and glistening

white lesions of miliaria, the rash being sharply demarcated at the wrist and not extending onto the hands (Tidy BMJ 63, 1943; Zinsser Rats, Lice and History Little, Brown & Co., 1935)

**Anhidrosis** is the absence of sweating partial or absolute It may be due to either insufficient function or deficiency destruction or absence of secretory apparatus. Anhidrosis is symptomatic in ichthyosis, ectodermal defects (q v) extensive psoriasis, scleroderma, morphea and other cicatricial lesions, including roentgen dermatitis in avitaminosis A, dehydration, atropine poisoning and in contact dermatitis due to astringent chemicals, including formol and other agents capable of producing squamous dermatitis.

Anhydrosis is also caused by lesions of the sympathetic nervous system. Local lesions in the cord medulla and pons and of the sympathetic system cause circumscribed loss of thermoregulatory sweating List and Peet (AMA ArchP 39 1228 40 27 1939; 1093, 1939) demonstrated Typical areas of anhidrosis occur after various forms of sympathectomy Postganglionic sweat fibers, contained in gray rami communicantes, supply the skin in segments roughly corresponding to the sensory radicular innervation. The location of lesions in the sympathetic nervous system can be delineated by investigations of thermoregulatory sweating



Fig 1016 — V id pa of h t sah f f following resection of left superior cervical ganglion L 1 ) (\ bel 1.38 40 1938.)

Generalized acq ed anh 1 osis (reated Engelhardt nd Mel m (AmJMSc 10 322, 1943) bose patient olera f h t for 13 ears and did not sweat even when heated t al temper t f 1 3 F Minor test sho ed sweating only in axillary term l and pe anal eg ons and histologically the sweat glands were atrophic

In the treatment f anh 1 os usuall method of atta k exists. I the generalized f rms, such ith ut (q the best that can be hoped for is temporary alleviation. The wea g t tt w no bathing, and the daily application of bland, soothi g l hn t ch pet olat m and h drous wool f t will serve t protect the skin V t m A nd perhaps th roid ma be indicated.

**Determination of Existence and Distribution of Sweating.**—Minor test paint the test area, after thoroughl lea ing and drying it, with a mixture of iodine 1.5, castor oil 10.0 and absolut alcohol 100.0. Onto the skin, which now looks

and yellow dust fine rice powder pressing it into pores with a soft cotton powder puff and fanning away the excess. The white and ivory-appearing skin manifests fine blue-black dots at points where sweat appears; such dots soon coalesce. Dripping spoils and terminates the test. The material is easy to wash off with soap. Using Minor s test, List and Peet (1938) investigated these types of sweating

THERMOREGULATORY—manifested in response to external heat, hot drinks, aspirin;
EMOTIONAL—elicited by emotional strain, or pain
MEDICINAL—elicited by pilocarpine (12 to 16 mg. by mouth) or Mecholyl (12 to 25 mg. by mouth) [*have ¼ gr atropine hypodermic ready as antidote*];
GUSTATORY—elicited by spicy foods;
SPINAL REFLEX—in transverse and other lesions of the cord.

They found variations in intensity and course and time of onset of sweating in normal persons, but symmetry is normal. Sweating is greater in folds and grooves, the axillary antecubital, inguinal, and submammary regions and it is less over prominent parts, such as the tip of the nose elbow knees, and extensor surfaces. Points can be found at all levels n the central nervous system, from the cerebral cortex to the peripheral nerve endings at which irritation may cause sweating.

## THERMOGENIC ANHIDROSIS (TROPICAL ANHIDROTIC ASTHENIA)

Atypical heat stroke was described by Wolkin et al. (J 124: 478 1944) and Blank (J 1 4 115. 1944) The subjects were soldiers enduring desert maneuvers who would manifest increased sweating of the neck and face and anhidrosis and cutis anserina below the neck level. Weakness, dizziness, headache tremor and subjective warmth followed, and the skin became warm and dry from the neck down. Hyperpyrexia and coma did not develop nor was there increase of pulse or respiration. Administration of salt was ineffective and pilocarpine and Mecholyl would not induce sweating until the patient had recovered by resting in a cool climate. The disorder came on rather suddenly, was preceded by hyperhidrosis for a few days or weeks, and responded promptly to a change of the conditions under which it appeared.

The syndrome differs from heat stroke, which is characterized by collapse delirium irritability visual disturbances preceded by nausea and vomiting, occurring often with dramatic suddenness, and manifested objectively by psychic changes, hot dry skin hyperpyrexia rapid pulse and increased depth of respiration. It differs also from heat exhaustion, which is manifested by headache drowsiness, extreme weakness, visual disturbances vomiting, vertigo and inability to walk with cramps of limb and abdominal muscles, cold and clammy skin, dilated pupils, fast pulse diminished blood pressure and temperature ot increased or increased only slightly

In atypical heat stroke the face became flushed when hot drinks were imbibed, and the skin showed a scaly fine papular rash on the extensor aspects of the extremities, superficial c rcinate areas of erythema with white scaling and mild pruritus. The patients f Novy (J 123 738, 1944) developed this disorder in a hot, humid climate. Fox (TransADA 1017) described histologic changes characterized by keratinous blocking of sweat follicles with or without cystic dilation of sweat glands, confirming the observations of Allen and O'Brien (MJAustral 2 335, 1944) 18 of whose 22 original cases had miliaria rubra due to corneous obstruction of sweat ducts.

The sweat retention syndrome may be divided into groups of cases (Sulzberger et al. JIn D 9 221 194 ) both showing signs and symptoms due t failure of sensible perspiration one due to plugging of glandular orifices, the other due to atrophy of the ducts. These phenomena may occur in atopic dermatitis, lichenoid Quinacrine eruption, and other conditions. See miliaria and sudamina.

## MILIARIA, PRICKLY HEAT AND SUDAMINA

**Miliaria** is an acute inflammation of the coil glands, characterized by the sudden appearance of small papules and vesicles, accompanied by sensations of itching and burning The malady usually develops in hot, sweaty weather While the lesions may be closely crowded together they never coalesce Ultimately they regress and undergo desiccation and desquamation. Their content is alkaline. The eruption may be of more or less generalized distribution but usually it is limited to the covered

parts of the body. Infancy, obesity, debility, over-clothing and a tendency to hyperhidrosis are predisposing factors. Uncomplicated, an attack usually subsides within a week. Mild and cool astringent lotions, such as dilute aluminum acetate or permanganate, supplemented by liberal applications of a bland dusting powder are helpful (Pollitzer: JCutDis 11: 50, 1893).

Miliaria, sudamina, and prickly heat were used as synonymous by Sulzberger and Emik (JInvD 7: 53–61, 1946). Their studies concerned military personnel on Guam, two-thirds of whom developed the disorder within a 7 months' residence there. Focal hyperkeratosis at the follicular orifices and diminished sweating in the affected regions were demonstrated. The sudoral pathology was interpreted as paralleling that of the sebaceous apparatus in acne vulgaris.

*Prickly heat and tropical anhidrotic asthenia are different manifestations of the same fundamental process* (Sulzberger et al.: JInvD 7: 153, 1946). Miliaria rubra represents the acute phase of sweat gland occlusion, with tiny glistening vesicles surrounded by red areolas; anhidrosis represents the chronic phase with occlusion, hyperkeratosis, and disappearance of inflammation (O'Brien: BJD 59: 125, 1947). If lanolin is smeared on the anhidrotic patient and he exercises, the greased area will sweat and no vesicles will arise there. The sweat glands are not atrophic or inactive, but sweat is resorbed as it is formed. The sweat duct dilates and later ruptures close to the level of the keratinous obstruction.

Treatment with salicylic acid in alcohol, causing desquamation, followed by applications of animal fat, is helpful. Best response is obtained if the patient is removed from the climatic conditions which cause his trouble.

**Sudamina** is the name given to a noninflammatory brief but abundant eruption of pinpoint to pinhead size superficial, thin-walled, translucent, pearl-like vesicles representative of coil gland obstruction. The lesions are whitish and closely set but they do not coalesce. Their content is acidic. They seldom rupture spontaneously but usually persist for a few days and then disappear by absorption.

## SWEAT GLAND NEOPLASMS

**Hydrocystoma** is a rare disorder characterized by discrete, tense, deep-seated, noninflammatory vesicles occurring in a localized patch usually on the face. The vesicles are deeply seated and never rupture spontaneously. In a few weeks the lesions undergo desiccation, leaving no trace. The disorder generally manifests itself during the summer months, and it *may recur seasonally. The cystlike formation* is a result of dilation of coil gland ducts. Roentgen therapy causes prompt and sometimes lasting disappearance of the lesions (Alderson: ADS 36: 1246, 1937).

**Syringoma.**—See p. 606; also Foot (1947) on p. 637.

## PECULIARITIES OF COLOR AND ODOR OF SWEAT

**Bromidrosis.**—Sweat secretion of an offensive odor may be due to functional disturbances or to alteration of the sweat after its excretion. The disorder may be general or local, and is usually associated with hyperhidrosis. The sweat of certain races is of noticeably different odor from that of others. The axillae, genitocrural regions, and the feet are the regions commonly involved. The secretion may be excessive, although not necessarily so. Odorosity of sweat is largely a function of the apocrine

glands. These do not evolve until pubescence and they degenerate in old age; the axillary odor of the adult is not present in the child or in the senile individual. Persons differ with regard to the general development and function of apocrine apparatus. Their odors are of variable strength, as well as variable in one person at different times.

The odors of various diseases are said to be recognizable such as pemphigus, uremia, measles, and carcinoma. Decomposing epithelium has a typical odor. Acne patients smell alike. Symmetric lividity of the soles (q.v.) is highly offensive. Estrus in animals and menstruation in human beings induce odorific alteration. Subjective experience of odor which may be offensive and hyperosmia occur in disturbances of the olfactory tract and tumors of the hippocampal gyrus or uncinate process, and also in menopausal psychoses (Lederer: J 114: 631 1940). See also foetor oris.



Fig. 1017



Fig. 1018.

Fig. 1017.—Hydrocystoma, lesions on forehead.
Fig. 1018.—Hydrocystoma, histology.



Fig. 1019



Fig. 1020.

Fig. 1019.—Uridrosis in uremia.
Fig. 1020.—Localized hyperhidrosis, cause undetermined.

Control of body odor may usually be accomplished by simple hygiene. Chemicals for topical application to control sweating include methenamine 0.5 per cent in a tragacanth lotion (Park: ADS 48 539 1943), salicylic acid 2 per cent in a powder, which perhaps adding sodium hexametaphosphate 5 per cent (BMJ 1: 703 1945); and such astringents as aluminum phenol sulfonate, aluminum chloride and zinc phenol sulfonate

in a cold cream vehicle (Weiss and Marcus: ADS 43: 859 1941) Baking soda powdered under the arms does not stop sweating but deodorizes (Lamb: JHarD 1 131 1946) See also J 119: 1406; and Eller (MRec 154 167 1941)

Chromidrosis is an affection characterized by the excretion of colored sweat. True chromidrosis is an extremely rare disorder Pseudochromidrosis is caused by the presence of chromatogenous microorganisms or various tinctorial substances on the surface of the skin (see trichomycosis flava, nigra, rubra) The discoloration is usually brownish, grayish bluish, or violaceous The secretion commonly collects slowly on the skin, and imparts to the affected areas a greasy powdery appearance, such as might result from applying lead pencil dust to a seborrheal surface. The pigment is mixed with grease; though only slightly soluble in water it can be removed readily with the aid of benzine or ether See Heidingsfeld (J 39: 1519, 1905) Samberger (DWehs 109: 898, 1939 also BJD 52 64, 1940) Murray (ADS 41 379 1940) gold sweat, colored tears.

Hematidrosis is an extremely rare disorder characterized by excretion of blood or blood pigment through the sweat glands. It is usually a manifestation of purpura. The disorder may involve limited areas on the face ears, umbilicus, or limbs, and the discharge may be preceded or accompanied by pain of a neuralgic character At times the condition is associated with other bleeding stigmas, vicarious menstruation and similar conditions.

Uridrosis denotes the excretion of sweat containing abnormal quantities of urinous elements, particularly sodium chloride and urea. It occurs in uremia, sometimes. After evaporation of the fluid constituents, the excreted material appears on the surface as a hoar frost-like coating, consisting of whitish crystals and irregular powdery masses.

Phosphoridrosis is extremely rare. Its occurrence has been noted in malaria, cancer of the breast, pulmonary tuberculosis, and following the ingestion of fish. It is possible that the phosphorescence has been due to photobacteria.

## SYMMETRIC LIVIDITY OF THE SOLES

The condition is characterized by the presence of macerated, wet, whitish or bluish-red, slightly elevated, sharply defined, bilaterally symmetric plaques on the soles, usually involving the heels and about one-third of the adjacent plantar surface as originally described by Pernet (BJD 37 123 1924) There is hyperhidrosis, and the skin appears edematous and sodden but vesiculation is absent Symmetry is not invariable The patient complains of tenderness. Parkhurst (ADS 27 962 1933) described 2 examples, and 25 per cent aqueous solution of aluminum chloride proved helpful in both.

While local hyperidrosis is an important factor the strong fetid odor typical of these cases, which are not rare, indicates that a fermenting agency is also concerned. Hitch and Hansen (ADS 38 881 1938) however could not find fungi in scrapings or cultures from 4 cases Their histologic study showed parakeratosis and hypergranulosis, edema, vascular dilation and moderate inflammation mainly perivascular Symmetry of location made them think of neurologic relationships. Kalz and Friedman (CanadMAJ 51 252, 1944) found the excessive sweat highly acidic

Treatment which is effective includes x ray therapy the wearing of properly fitting lightweight footwear and a salicylic acid and sulfur salve such as would be suitable for tinea and which stops the bad odor satisfactorily Nelson (ADS 47 822, 1943) recommended an astringent powder and h3ln0 socks. Hopkins et al (ADS 57 850 1948) thought well of 5 per cent paraformaldehyde in talc or bentonite.

## GRANULOSIS RUBRA NASI

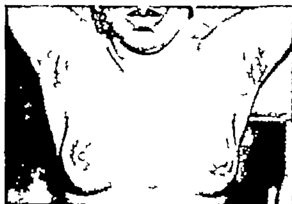
This is a chronic disease of the alar regions, characterized by congestion, hyperhidrosis, and well-defined, reddish, pinpoint to pinhead size vesicles and papules. Cases occur generally in delicate children Hyperhidrosis is the constant feature and often

includes the upper lip, cheeks, forehead, and even the entire face, and also the palms and soles. The redness is diffuse, poorly defined, bright or dull in intensity disappearing on diascopy. Telangiectasis is occasionally present. The papules are round, closeset, soft and distinct, never confluent. Pores are not present at their apices. Sometimes they are umbilicated and minute pustulation may exist. Scales and cicatrices are absent. Association with cold, cyanotic hands and feet is common. Abortive cases without papules are sometimes seen. Symptoms are practically wanting. There is no tendency to ulcerate. The cause is unknown. There is some evidence that granulosis rubra nasi can be inherited. The disorder is a chronic and persistent one, but tends to disappear on the approach of puberty. Internally cod-liver oil and iron have been recommended. Locally astringents may be tried, and x rays prove curative in many instances (Beeson, ADS 14, 256, 1926).

## DISORDERS AFFECTING THE APOCRINE GLANDS

### LICHENOID ERUPTION OF THE AXILLA

**Lichenoid Eruption of the Axilla (Fox Fordyce Disease)** is a rare chronic, itchy disorder involving the axillae in women, sometimes affecting also the pubic, sternal and areolar regions. The papules comprising the eruption are closely grouped and dry. Itching is the earliest symptom and is sometimes almost intolerable. The lesions develop slowly and do not



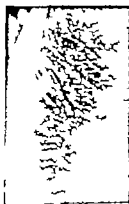


Fig. 1021 and 1022.—Fox Fordyce disease in a young Negro woman, showing axillary, sternal, and areola distribution, pubis also affected. Plastic surgery eventually relieved the patient.

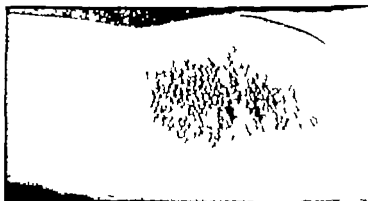


Fig. 1023.—Fox Fordyce disease, axilla.

regress spontaneously (Fox and Fordyce JCutDis 22 1, 1902) The cause of the disease is unknown. The inflammation surrounds apocrine glands (Way and Memmesheimer ADS 38 377, 1938) Roentgen therapy is a mode of attack of only fair effectiveness, but topical applications accomplish almost nothing In cases not helped by x ray one may inject the subcutis with 95 per cent alcohol. Endocrine treatment disappointed Cornbleet (ADS 54: 225 1946) but Roxburgh (BJD 55 121 1943) reported benefit with stilbestrol. Plastic surgery may be recommended in some cases.

## HIDRADENITIS SUPPURATIVA

**Hidradenitis Suppurativa** (apocrine acne [some cases] or apocrine furunculosis [some cases]) is characterized by deeply seated acneform inflammation of the apocrine glands, particularly of the axilla but also elsewhere. It may lead to suppuration. Two diseases, in our opinion, are seen manifesting abscesses of the apocrine sweat glands.

**Apocrine Acne.**—Brunsting (ADS 39: 108, 1939) described the disease as essentially one of adult life. It affects robust persons who are well nourished and developed. It occurs without associated systemic disturbance or impairment of the general health, excepting, we note the lassitude of the hypothyroid individual, the tendency to obesity and the concurrent acne in 7 of Brunsting s 22 cases. Early lesions are a few small, firm, reddish, tender nodules. These increase in number and size and often coalesce to form typical cordlike bands. The pain they produce is variable, and it may be so considerable as to limit mobility of the shoulder joint. Some nodules resorb, wholly or only partially leaving comedones, sebaceous cysts, pitted scars, and bridge scars. Some suppurate indolently with foreign body reaction. Perianal pyoderma is hidradenitis (Marks BMJ 39: 477 1946) See acne conglobata.

**Apocrine Furunculosis.**—This type of hidradenitis, which may be primary or more often secondary to apocrine acne, is the manifestation of acute or chronic relapsing painful, pyogenic infection. Forming cherry size, pus-containing lumps, their thick, greenish yellow purulent content usually finds egress at the surface, but it may burrow and form intercommunicating subdermal sinuses. Remissions and relapses may occur and healing may be delayed for several months. Fever and associated systemic reaction in connection with recurrent bouts of regional cellulitis are common. About the anus, extension of the disease process through the deep tissue may continue so as eventually to perforate the rectum and to form anal fistulas. Primary hidradenitis is often incited by staphylococci abetted by the application of an ointment to the axilla.

Each patient presents an individual therapeutic problem. In the chronic state, when recurrences of acneform lesions are annoying but not disabling, the best treatment is as for infected acne with low fat diet, thyroid extract, penicillin and roentgen therapy Cysts may be excised, or simply let alone. No ointment should be applied to the region. A lotion, such as 1 per cent phenol with 1:5,000 bichloride of mercury in 70 per cent alcohol, is useful for topical application. When the disease has caused gross deformity plastic surgery is required. When pyogenic infection is active, treatment must meet the surgical indications. Excision may be advisable Rest incision and drainage, Dakin s solution, radiant or moist heat, roentgen therapy staphylococcus toxoid, sulfonamides, penicillin and sedative medication may be used as needed (Tachau: ADS 40 595 1939)

## DISORDERS AFFECTING THE SEBACEOUS GLANDS

### ASTEATOSIS

**Xerosis** is a condition characterized by deficiency of sebum. As a primary disturbance, it is associated with ichthyosiform and hypotrichotic ectodermal defect. Symptomatic hyposteatosis occurs in senility avita

minosis myxedema, diabetes scleroderma, xeroderma pigmentosum, ichthyosis, leprosy glossy skin, scars of burns, roentgen dermatitis, pressure atrophy and the kind of dermatitis due to fat solvents, alkalies, such as strong soaps and washing powders, and other astringent or inspissating agents, such as alum and formol. The last give rise to local, asteatotic dermatitis venenata, with dryness thickening loss of flexibility pruritus and fissuring (see p 75)

*Prognosis depends on the causative factor and on permanency and* degree of damage or deficiency of the sebaceous apparatus. Lubricants such as almond oil benzoinated lard, or mixtures of petrolatum and lanolin are indicated. Low humidity contact with wool and excessive use of soap are to be avoided. Compare xerostoma.

## FORDYCE'S DISEASE

The lesions are minute, pinpoint to pinhead size, whitish, yellowish, or chamois-skin colored tumors, which generally lie flush with the surface of a mucous membrane. Patches of considerable size may be formed The *inner surfaces and vermillion borders of the lips especially of the upper* lip frequently are affected (Fordyce JCutDis 14 413 1896) Within the mouth the site of predilection is about the opening of the parotid duct. We have seen cases involving the shaft of the penis, and the areolae of the nipples. Symptoms are usually lacking The tiny masses consist of anomalous, hypertrophic sebaceous glandular elements (Sutton JMRes 14 489 1914 Chambers ADS 18 666 1928) The condition is a common (Halter AfDuS 176 201, 1937) and harmless one. Discovery of its presence is usually accidental No treatment is necessary

## RHINOPHYMA

**Rhinophyma** is *characterized by the development of firm lobulated* thickened, purplish masses of rugose integument on the nose as a result of chronic and extreme seborrhea and hypertrophy of sebaceous glands. The tissue consists of enormous sebaceous glands, their ducts patulous and engorged with seborrheic material The course is slowly progressive Severe grades are almost restricted to men, and alcoholism is a common but not an invariable causative factor Symptoms are absent excepting the conspicuous deformity In advanced cases of rhinophyma resort must be had to plastic surgery (Klauder ADS 33 885 1936)

## ACNE VARIOLIFORMIS

**Acne Varioliformis** is a chronic, inflammatory disorder characterized by the development of a few or several reddish or brownish papulopustular lesions, which frequently involve the follicles and are always followed by more or less varioliform scarring The disease is comparatively rare The scalp forehead, nose and cheeks are favorite sites, although in rare instances the trunk and even the extremities, may be involved. The lesions are discrete or grouped pinhead to pea size papules or nodules, slightly elevated and pale reddish in color They develop slowly and ultimately undergo central necrosis and occasionally pustulation, with the formation of brownish adherent crusts Within a few days the crust becomes detached, and atrophic scarring is exposed Typical cases are almost asymptomatic The course of the disease is persistent and, with the

development of new lesions, may continue over a period even of years. Some authors consider the disorder a tuberculid others attribute it to *Staphylococcus pyogenes* The disease is to be distinguished from acne vulgaris and pustular syphilis (Sulzberger ADS 38 122, 1938) Untreated, it may persist indefinitely and relapses and recurrences are common. Internally measures looking to the improvement of the patient's resistance to infection are indicated. Staphylococcus toxoid and salicylic acid and sulfur ointment helped a patient of Crawford (ADS 40 106 1939) Bacteriophage and liver injections apparently cured a case of Bechet (ADS 36 897 1936, 41 969 1940) Roentgen therapy yields temporary disappearance of the disease Penicillin by injection is helpful

## NEW GROWTHS INVOLVING SEBACEOUS GLANDS

See sebaceous cyst (p 609) milia (p 610) adenoma sebaceum (p 604) sebaceous carcinoma (p 605) and pathology of basal-cell carcinoma (p 637)



Fig. 1024.



Fig. 1025.

Fig. 1024.—Rhinophyma. (Dr Grover Wende.)
Fig. 1025.—Hypertrophic fat gland.



Fig. 1026.—Acne varioliformis. (Dr I. R. Pels.)



Fig. 1027.—Milia of eyelids.

# DISEASES OF MUCOSAE ADJOINING THE SKIN

Diseases of mucosae constitute as broad a subject as diseases of skin. Mucous membranes adjoining the skin may be considered, for purposes of dermatologic thought, as simply thin skin modified by these conditioning features (1) mucosae are more or less continuously wet (2) they are covered with stratified squamous epithelium which normally does not produce a stratum corneum (3) they lack hairs, but do not necessarily lack sebaceous glands (see Fordyce's disease); (4) they lack coil glands, but, in the mouth particularly they are provided with mucous glands and (5) mucosae are so located and arranged with respect to underlying structures that their hazards, contacts, and parasites are somewhat different from corresponding cutaneous ones.

**Similarities of Mucosal and Cutaneous Disorders** are notable:

Mucosal tissues are susceptible to mechanical, chemical, and allergic disturbances

Mucosal tissues may be superficially infected with transitory parasitism which leaves no trace or inoculated with the chancres of various infections or deeply infected with ulceration which results in scar

Mucosal tissues are damaged as the skin is by systemic parasitism so that syphilis, leprosy tuberculosis and other systemic diseases provoke mucosal lesions. Mucosal tissues are altered by metabolic processes, including xanthoma and various avitaminoses, much as the skin is.

Mucosal epidermis may be malformed like that of the skin, with ichthyosiform nevi, and mucosal mesodermal tissues are susceptible to hemangiomatous, neurofibromatous, and other malformations.

Mucosal blastomas include epidermal carcinoma, glandular neoplasia, and sarcomatous lesions, and these may be primary or secondary

**Conjunctival Lesions** are described elsewhere in connection with caterpillar dermatitis congenital ectodermal defect contact dermatitis, diphtheria, dermatitis medicamentosa, erythema multiforme, eruptive stomatitis, gonorrheal dermatoses, hemangioma, ichthyosis, lupus vulgaris measles, pemphigus, purpura, sycosis, tularemia.

**Ocular Apparatus** is of dermatologic concern in albinism, atopic dermatitis, avitaminous dermatitis medicamentosa, hemangioma, melanoma, pemphigus, sarcoid syphilis t berculosis.

**The Eyelid** offers 3 dermatologic regions external skin, margin and conjunctival surface These are so close together that disease of one is likely to affect the others. Lesions described elsewhere include (1) primarily cutaneous abscess, alopecia areata, carcinoma, cysts, dermatitis medicamentosa, dermatitis venenata, erysipelas, exfoliative dermatitis, ichthyosis, keratosis senilis, milium, molluscum contagiosum, scurvy trichinosis urticaria, wart xanthoma; and ( ) primarily marginal: furunculosis (stye) phthiriasis rosacea seborrheic dermatitis, ariboflavinosis. See pp. 30 and 622.

**Nasal Mucosal Lesions** are described elsewhere with iodism. diphtheria, furunculosis of vibrissae leishmaniasis, purpura, rhinoscleroma, streptococcic fissure syphilis, telangiectasis, t berculosis, and yaws.

**Penile Mucosal Lesions.**—Here are included the mucous membranes of the glans prepuce and urethra. The urethra is omitted from consideration. Lesions are described elsewhere in connection with carcinoma chancroid, condyloma acuminatum dermatitis venenata, eruptive stomatitis, gangrene herpes simplex, kraurosis lichen planus, lichen sclerosus, lymphogranuloma inguinale scabies, syphilis, errors and Vincent's infection.

**Mucosae of the Female Genitalia.**—Lesions are described elsewhere in connection with acanthosis nigricans, vitamin A, carcinoma syringoma, dermatitis medicamentosa dermatitis venenata, erythema multiforme herpes simplex, hidradenitis, kraurosis, leucoplakia, lichen planus lichen sclerosus, lymphogranuloma inguinale moniliasis, oxyuriasis, pellagra pemphigus, pruritus, streptococcic vaginitis syphilis trichomonad infestation, verruca

Anal Mucosal Lesions are described elsewhere in connection with acanthosis nigricans, amebiasis, carcinoma, fistulas and sinuses, hidrosadenitis, lichen planus, moniliasis, oxyuriasis, pruritus ani, syphilis, tinea, and tuberculosis cutis orificialis.

## ORAL MUCOSAE

Disturbances may be classed by location and by type, and descriptions of oral mucosal lesions may be ordered accordingly with descriptions of each type of lesion in each location

| LOCATION AFFECTED | TYPE OF LESION |
|---|---|
| Mouth, in entirety or in part | Malformation |
| | Neoplasia |
| | Primary |
| | Secondary |
| Teeth (ectodermal) | Injury |
| | Trauma |
| | Physical agency |
| | Chemical agency |
| Lips, particularly | Local Inflammation |
| | Allergic |
| | Nonspecific, presumptively parasitic |
| Gums, particularly | Specific parasitism |
| | Systemic Inflammation |
| | Allergic |
| | Nonspecific, presumptively parasitic |
| Palate, particularly | Specific parasitism |
| | Metabolic Disturbance |
| | Pigmentary Disturbance |
| Tongue, particularly | Nervous Disturbance |

Teeth are ectodermal structures of dermatologic concern in conditions described elsewhere congenital ectodermal defect, focal infection, galvanic lesions due to fillings, granuloma pyogenicum, sinus tracts of dental origin, and congenital syphilis.

## MALFORMATIONS

Mouth.—Clefts of various types, primarily of surgical interest, result from failures of embryologic development and fusion. Ichthyosiform nevi comprise one type of leucoplakia. The oral ectoderm, including the teeth, is defective in congenital ectodermal defect. In epidermolysis bullosa, mucosae may be abnormally vulnerable, as is the skin (Forman BJD 58 26, 1946) Cavernous or macular hemangioma may affect the mouth, often in accompaniment with extensive facial hemangioma. Cavernous lesions, with lymphangioma and hypertrophy result in macrocheilia, macroglossia, macromelia, and distortions and disproportions. Telangiectasis affects particularly the undersurface of the sides and tip of the tongue, but also other parts of the mouth the little capillary ballooning, reddish purple, soft, and multiple, may rupture and cause more or less severe hemorrhage (Osler s disease) V Recklinghausen s tumors, particularly neurinoma, affect the mouth (Martin and Graves J 117 1535 1941) these firm, pinkish or whitish, sessile or pedunculated, benign tumors are found about the lips and tongue. Macromelia is hypertrophy of the cheek, macroglossia is hypertrophy of the tongue, and macrocheilia is hypertrophy of the lip These are sometimes congenital, sometimes slowly progressive. In treating these lesions, plastic surgery is the only recourse. Commonly they are best let alone.

**Lips.**—Fordyce's disease fistulas of the lips, and capillary varices are described elsewhere.

**Cheilitis Glandularis Apostematosa** is a chronic disorder of the lips, characterized by swelling due to hypertrophy of the mucous glands and their ducts, with secondarily inflammatory symptoms of variable degree.



Fig. 1028



Fig. 1029.

Fig. 1028.—Cheilitis glandularis apostematosa. (Sutton JCutDis 27 150, 1909)
Fig 1029 —Cheilitis glandularis apostematosa hypertrophic duct of mucous gland of lip.



Fig 1030



Fig. 1031

Fig. 1030 — Scrotal tongue (Dr Howard Fox.)
Fig 1031 —Glossitis rhombica mediana. (Abahler ADS 30 409 1931)

When the lower lip is everted, one sees widely dilated sievelike openings, irregularly scattered over the vermilion border Abscesses have developed in such glands, but this complication is unusual. There is generally an associated hypertrophy of the mucous glands of the buccal and pharyngeal mucosa, and of the tissues of the turbinates and tonsils.

so that catarrh is common. It is a congenitally excessive supply of glandular tissue in the nose, pharynx, mouth, and lips. It is not 'pre cancerous (Sutton InternatClin 3 123, 1914)

**Gums.**—Malformations here are particularly those occurring with clefts and malformations of the teeth

**Hypertrophy of the Gums** is a curious deformity which shows an hereditary tendency Its onset is early in life Both jaws are affected as a rule. Involvement may be unilateral or bilateral. While the tissues look normal they are so excessive in quantity that they cause great deformity even actually covering the deciduous or permanent teeth giving rise to the so-called hippopotamus face (Hirschfeld JAmDentA 19 799 1932 Ruggles: J 84 20 1925) Mastication is hampered. This type of hypertrophy is distinct from hypertrophy due to xanthomatous infiltration such as occurs in Gaucher's disease, from neoplastic infiltration in leukemia, and from hypertrophy associated with pregnancy or irritation by dentures (Battaglia and Curphey AmJDisChild 57 1404, 1939) No success in treatment may be expected excepting by surgical removal of the whole abnormal mass, including the teeth, alveolar process, and soft tissues (Monash: ADS 24 580 1931)

**Palate.**—Malformations here include dysontogenetic clefts, angiomas which may bleed distressingly even though only a millimeter in diameter exostoses, and ecchondroses. The common midline bony or cartilaginous lump or crest, torus palatinus, is simply osseous excess at the line of union of the two halves of the palate. It is asymptomatic unless bruised.

**Tongue.**—Conspicuous congenital defects are rare Tongue-tie or shortness of the frenum is seen; usually it should be let alone particularly in infants Hypermobility has been recorded as also have absence of the tongue, cleft tongue and microglossia. True grooved tongue or scrotal tongue is a congenital malformation sometimes hereditary (Tobias ADS 52 266 1945) The grooves are plications of redundant mucosa. Annoying fissures may develop in them A condition like scrotal tongue may result from inflammatory hypertrophy and edema or from syphilitic scarring Mammillated tongue is a rare condition, or rather collection of heterogeneous malformations (Weber BJD 57 179 1945)

**Glossitis Rhombica Mediana** is a rare asymptomatic lesion always located in the middle third of the dorsum of the tongue The surface is smooth, shiny and reddish There is slight induration. Usually the disorder is discovered by accident Nothing is known of its etiology and no treatment avails except excision or destruction The tissue excess is neither inflammatory nor neoplastic (Martin and Howe AnnSurg 107 39 1938) Treatment is not necessary

## NEOPLASIA

**Retention Cysts** of the mucous membrane often involve the lips, the common location being in the inner aspect of the lower lip at a point adjacent to the left cuspid. The lesions are somewhat paler than the normal mucosa because of their mucinous content and their expansile pressure. They are painless If incised, they refill as soon as the wound heals. They must be completely removed (Sutton JCutDis 36 579 1918)

**Ranulas** are bluish cysts situated beneath the tongue, allegedly due to obstruction of the sublingual ducts. They may involve one or both

Fig. 1032.—Retention cyst of lip.

Fig. 1033.—Leucoplakia superficial carcinoma.

Fig. 1034

Fig. 1035.

Fig. 1034.—Leucoplakia of tongue. (Dr. George M. McKee.)
Fig. 1035.—Leucoplakia superficial carcinoma. (Dr. Fred Weidman.)

Fig. 1036

Fig. 1037

Figs. 1036 and 1037.—Giant cell epulis. (Hynes, L. V.: Clinical Diagnosis [illegible] Dental Items of Interest Publishing Co., Inc.)

sides of the midline and the size may be so great as to interfere with phonation and eating

**Epithelial Pearls** of pinhead size are occasionally seen along the median palatine raphe in the newborn. These milia require no treatment.

**Epulis** is any growth involving the gums (Anderson ASurg 38 1030 1939)

**Giant-Cell Epulis** is a benign tumor which recurs if its removal is incomplete These are of pea to hickory nut size, as a rule, but may be considerably larger especially in the upper jaw They form rounded tumors between or about one or several teeth. They generally arise about a single tooth, and may spread and extend so as to involve adjacent teeth. The color is generally that of the surrounding mucosa which is under grown by the tumor Giant cells are remarkably prominent in the histologic structure, and the more malignant one is, the fewer the giant cells. To cure these their bases being attached to the root of one or more teeth, it is necessary to sacrifice the tooth or teeth along with the border of the alveolar process and sometimes considerably more. Rarely they are malig nant (Sachs and Garbe ADS 38 603 1938)

**Fibrous Epulis** is local hypertrophy of the mucosa, nevus, neurilemmoma, or fibroma.

**Angiomatous Epulis**, a soft red lesion, is granuloma pyogenicum.

**Thyroglossal Cysts** are cysts located in the midline of the tongue anterior to the epiglottis, due to dysontogenesis of the thyroglossal duct. Fistulas also occur (Kinsella BJS 26 714, 1939)

**Thyroid Tumors of the Tongue** are interesting curiosities. The tumor firm and elastic, is composed of thyroid glandular tissue, and located centrally at the base of the tongue. It is functionally active as a rule. It may contain all the thyroid tissue the patient has (Ray ASurg 87 316 1938 Lemmon & Paschal AmJSurg 52 63, 1941)

**Leucoplakia** is whiteness of the mucous membranes, which normally look pink. The whiteness exists because the avascular epidermal layer is abnormally thick for some reason or other Leucoplakic areas may be thick or thin, smooth or rough, sharply demarcated or fading at the border single or multiple, discrete or confluent, and widely spread over the mucosa or narrowly delimited.

**Neoplastic Leucoplakia** is the mucosal analogue of the cutaneous keratosis, and intergradient degrees of malignancy exist. Leucoplakic intraepidermal neoplasia and squamous intramesodermal carcinoma are distinguished only by time intervals and location of cancer cells. Neoplastic leucoplakia is superficial carcinoma. Injuries may give its cells access *into connective tissue. When normal epithelium* and abnormal epithelium grow side by side, the normal, under favorable circumstances, may supplant it, replace it, and recover the once abnormal area, so that the patch is gone for good, just as keratoses similarly may disappear One sees this particularly when the patient with chronic tobacco irritation and smokers patches gives up smoking and some—perhaps all—of his leucoplakic lesions peel off and disappear within a few weeks. Those which remain after 2 months are dangerous and must be thoroughly destroyed. Neoplastic leucoplakia is irregular in outline but always is sharply mar ginated. The thicker it is, superficially set on the mucosa, the less instant is its danger in general. Thin, flaky easily bleeding leucoplakia, like the analogous keratosis senilis, is dangerous erythroplakia simply requires



Fig. 1032.—Retention cyst of lip.



Fig. 1033.—Leucoplakic superficial carcinoma.



Fig. 1034



Fig. 1035

Fig. 1034.—Leucoplakia of tongue. (Dr. George M. M[illegible].)
Fig. 1035.—Leucoplakic superficial carcinoma. (Dr. Fred Woldman.)



Fig. 1036



Fig. 1037

Figs. 1036 and 1037.—[illegible] cell epulis. (H[illegible], L. V.: *Clinical Diagnosis of Diseases of the Mouth*, [illegible] Publishing Co., Inc.)

teeth. The papillae are greatly enlarged, the gingival tissues are soft and succulent, salivation is profuse, and excoriation and infection of the gums lead to bleeding, soreness, and fetor Noma may terminate acute leukemia.

**Polycythemia** causes purplish redness of mucosae and, occasionally hemorrhages from gingival papillae

**Sarcoma** of the mouth may be primary Tonsillar lesions sometimes develop so rapidly into fungating, ulcerous masses with cervical gland metastases, that one suspects infection instead of blastoma. Mycosis fungoides may manifest oral lesions. Kaposi s sarcoma often does. Osteosarcoma, antrum tumors, tumors of the jaw adamantinomas, radicular cysts, and dentigerous tumors are merely mentioned here Fibroma, lipoma, myoma, angioma and neurofibroma (q v ) may occur in the mouth. Melanoma of the palate was noted by Arons (Laryng 49 271, 1939) chondroma of the tongue by Johns (JMichSMS 41 471 1942) primary lymphosarcoma of the palate by Freeman (AmJR 43 702, 1940)

## INJURIES

**Trauma.**—Lesions such as cuts, fractures, gunshot wounds, foreign bodies including bones of fish, and the like are mentioned. Cheilitis is often due to sucking the lower lip Pressure sores of the lips may follow manipulations by dentists who lean on the lip instead of the teeth.

**Cotton roll gingivitis** is the name for gingival damage which results from applying dry absorbent pads to the gums and pulling them away without first moistening them so that epidermis adheres to the pad and is torn off.

**Local Hypertrophy** of the gingival tissues or of the mucosa of the inner surface of the lip may form locally in response to suction or to distortion by dentures. The lesion is a whitish or pinkish, firm, asymptomatic benign mass, covered with epithelium, composed of edematous fibrotic tissue, resting on an uninflamed base which is not indurated.

**Adenoma of the Mucous Glands of the Palate** is a disturbance generally due to suction and hypertrophy induced by the wearing of an upper plate. One sees a bosselated group of asymptomatic smooth, pinkish, hemispheric nodules on the palate (Ronchese ADS 36 1222, 1937)

**Bednar s Aphthae** are excoriations occurring generally symmetrically on the sides of the rear of the hard palate. They arise from thumb-sucking or from lollipops or scalds They heal when the provocation ceases.

**Ulceration of the Frenum** of the tongue occurs with severe coughing especially in whooping cough.

**Decubital Ulcers** result from ill fitting prostheses and fillings, from malformations or distortions of the jaws or teeth from rough edges of *carious lesions, and from pipestems and other foreign bodies.*

**Perforating Ulcer** in the palate is generally due to syphilis. Perforating ulcer may occur in syringomyelia, leprosy encephalitis, yaws, leishmaniasis, and chromium poisoning. Treatment depends on the cause

**Actinic Cheilitis** occurs in the summertime as a rule, affecting the person whose integument is sensitive to the sun's rays. The lips are swollen, sometimes considerably, and the vermilion surface, especially of the lower lip is scaly fissured, and more or less crusted. This is relieved by staying indoors or wearing a broad-brimmed hat and a thick layer of zinc paste as a sun screen (Ayres J 81 1163 1923)

Burns of the lips and mouth are commonplace generally resulting from taking food while it is too hot Therapeutic burns are made to destroy tissues such as leucoplakia. Burns range from first to third degree. They heal promptly if the mouth is simply kept clean, and if the mucosa is not irritated by medicinal agents.

**Galvanic Lesions** of the mucous membrane were described by Lain (ADS 41 295 1940) as resulting from the electric current which passes through saliva and oral tissues, serving as electrolyte when fillings of *dissimilar metals are present in one mouth. The metal ions moving in* this current may cause stomatitis venenata We never saw a case.

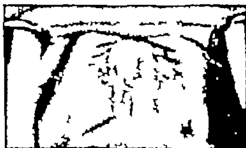


Fig. 1038.

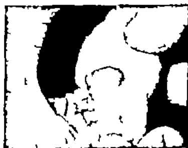


Fig. 1039.

Fig. 1038.—Hypertrophy of mucous gland of palate. Such condition may result from suction due to ill-fitting denture (Hayes L. V. *Clinical Diagnosis of Diseases of the Mouth* Dental Items of Interest Publishing Co., Inc 1932.)

Fig. 1039.—Fibrous epulis local hypertrophy of buccal mucosa probably due to ill-fitting denture (Dr Erwin Zeisler.)



Fig. 1040.



Fig. 1041.

Fig. 1040.—Swelling of mucous gland ducts of the palate of a smoker (Ronchese ADS 36 1222, 1937.)

Fig. 1041.—Lesion like those in Fig. 1040 in a woman who totally abstains from tobacco. Note also torus palatinus (Dr F Ronchese.)

**Roentgen and Radium Injuries** may occur within the mouth Damage of the lip is a price one perhaps willingly pays for cure of carcinoma. One may excise the distressingly tender and sensitive, atrophic and telangiectatic sometimes ulcerated tissue and so give immediate re-

lief. Xerostoma from roentgen treatment of lesions of the face is sometimes seen. Roentgen injuries of teeth were discussed by Regato (AmJR 42 404, 1939) Results of absorption of radium, including osteosarcoma of the jaw were discussed by Evans and Aub (AIntM 11 1443 1938)

**Chemical Injuries** of the mouth may be suffered from acids, alkalies, and caustics, such as copper sulfate phenol, iodine, and other agents. The extent of the injury primarily determines its significance. Ulcers heal readily within the oral cavity if the individual survives his poisoning. Damage done to the pharynx and esophagus is important for perforation leads to death, and cicatrization leads to serious difficulty. Emergency treatment consists in generous lavage with water using weak dilutions of vinegar for lye, or bicarbonate of soda for acids—one depends mainly on lavage. Lemon juice habitually imbibed is capable of dissolving off the enamel and producing extensive dental damage (Stafne and Lovestedt PSMMC 22: 81 1947) See also stomatitis venenata.



Fig. 1042.



Fig. 1043.

Fig. 1042.—Dental lesions following roentgen therapy of cancer of oropharyngeal tissues. (Regato AmJR 42 404 1939.)

Fig. 1043.—Cheilitis such as may be caused by eczematous sensitivity (Dr W Herbert Brown.)

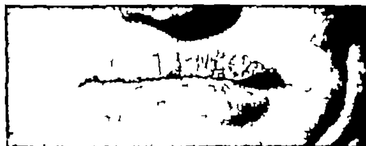


Fig. 1044 —Actinic cheilitis.

**Tobacco Stomatitis** is a form of chemical injury Actual hypersensitivity is apparently excessively rare. In the ordinary irritation, the mucosa is red and injected, and the mucous glands pour out excessive amounts of secretion, which leads to pharyngeal droppings, hawking and

cough. It is possible that benefit may result from changing the brand of cigarette to one using diethylene glycol instead of glycerol better is to stop tobacco

The tarry distillate of the smoldering woody stuff is keratolytic as salicylic acid is, and the mouths of some persons become the seat of extensive, inflammatory exfoliating leucoplakia. Distinct from neoplastic leucoplakia, irritative leucoplakia fades gradually at the margin into unaffected tissue, lacking a definitive border The combination of suction and irritation produced by smoke leads often to enlargement and minor inflammation of the mucous glands of the palate, and the tissues about their orifices called adenoma of the mucous glands of the palate (q v ) or papular leukoplakia of the mucous gland ducts (Cummer J 132 493, 1946)

**Xerostomia,** or dry mouth, occurs when the salivary glands are atrophic as a result of congenital aplasia of the salivary glands, avitaminosis A or the influence of roentgen rays. It occurs when the individual ingests little fluid perhaps because of sore mouth, esophageal constriction, or sore urethra. Fever dehydration, diuresis, and belladonna are other causes. The dried mucosa is especially susceptible to fissures, bacterial infection, and mycotic parasitism. It must be kept moistened by frequent lavages with physiologic salt solution. The vitamin B complex may be needed.

## LOCAL INFLAMMATORY DISEASE

**Stomatitis Venenata (Contact Mucositis).**—There is no substantial difference between hyperergic contact inflammation involving mucosae and dermatitis venenata (q v ) Contact damage typically is variable in intensity in relation with the noxa and its application flares indicate contacts, and continuous disease indicates continuous or frequently repeated contact Medicinal agents often irritate mucosae Oral manifestations of occupational origin were reviewed fully by Shour and Sarnat (J 120 1197 1942)

Cheilitis Venenata.—Cosmetics are usually to be blamed. The lesion is likely to be manifest with swelling scaling oozing unsightliness and discomfort, and its margin is a fading one rather than definitive as in lupus erythematosus. The process may be mild but persistent. Lips and face may be affected by sensitivity to the rubber of dentures. Lips may show mercurial dermatitis following the placing of an amalgam filling Various dentifrices have been caught causing trouble and mouthwash lipstick, perborate orange peel cinnamon oil chewing gum and even penicillin have been incriminated Soap shaving soap and aftershave lotions often irritate lips.

Gingivitis Venenata —The gums are swollen possibly flaky and oozing red and excoriated, particularly at the vulnerable tips of the papillae. The teeth may be sore and the discommodation is perhaps so great that eating is almost impossible. Irritation in the mouth is always accompanied by salivation Vincent s infection may attack the damaged tissues.

Stomatitis Venenata —While this affects a large proportion of the oral mucous membrane or all of it the tongue is generally considerably involved. The surface is redder than normal is more or less swollen and causes symptoms of sensitiveness, burning and tenderness. Flares occur when the contactant is of external source and is met only occasionally As in skin, contactant injury may be by primary irritants or sensitizers.

Foods are occasional sources of this trouble, especially chocolate, pecans, walnuts, and salty popcorn. We have seen cheilitis due to oranges. Medicines of cough drops, nose drops, tonics, breath purifiers, and whiteners of the teeth, along with synthetic chemicals of candies and flavorings, may be at fault. The cure of this disorder depends basically on the removal of something from the region, not on the application of medicines. The lips are comforted by cool moist applications of 1:500 aluminum acetate on a bit of cotton, a pack which may be laid on top of a layer of petroleum jelly. In the mouth, physiologic saline solution is satisfactory as a frequent tepid lavage, and no medicine at all works better than any other therapeutic agency. In the presence of infection gentian violet is as lacking in capacity for causing trouble as any we know. Some chronic cases prove very difficult, particularly when the lips alone are affected. A scalp lotion may be to blame. Moistening the fingers with the tongue allows any chemical one has touched to reach the mucosa, and investigation must be pursued much as in contact dermatitis. Technic for patch testing mucosae has been described by the Goldmans (ADS 50: 79, 1944) and Farrington (JInvD 8: 69, 1947).

**Nonblastomatous Leucoplakia.**—Any lesion in which there is proliferative superabundance of epithelium causes leucoplakia when it occurs in the mouth. In many kinds of stomatitis, the epithelial tissue tends to scale off and so to cover the papillae only thinly; in such lesions the mucosa is redder than normal, in contrast with leucoplakia. Plainly there is no one method of treatment applicable to all kinds of leucoplakia. An effort must be made to discover the cause. Since the leucoplakia of inflammation is different in significance and treatment from leucoplakia of neoplasia, the distinction is important. Much leucoplakia of the inflammatory type may safely be neglected, as "coated tongue" may be, as a rule. Often the cure rests on keeping something out of the mouth, mouthwashes included. Tobacco, walnuts, pecans, and chocolate are common causes. Syphilitic leucoplakia is distinguished by its thick, white patches, which are circumscribed, oval, usually crowded together in a mosaic, located on the dorsum of the tongue, and set on syphilitic glossitis. See also **kraurosis**, and the Plummer-Vinson syndrome.

**Catarrhal Stomatitis** is the title applied to "simple stomatitis" superficial in character, manifesting redness, mild desquamation, and either dryness or serous exudation. It may be eczematous or bacterial. It is synonymous with "mild stomatitis of undetermined cause."

**Marginal Gingivitis** is acute or chronic inflammation of the gum margins, affecting the papillae and the labial and lingual aspects of the gums. Causes include everything that may injure the gums, ranging from calculus through chemical irritants to leukemia and scurvy. "Marginal gingivitis" is a diagnosis as definitive as "sore leg."

**Atrophic Gingivitis.**—The gingival margins, including the slightly shrunken papillae, are retracted from the teeth. Pressure on the gum causes pus to ooze forth. Occasionally the teeth are loose. Symptoms are of foul breath and taste resulting from decomposition of debris and exudate. The patient is benefited by practicing oral hygiene. Avitaminosis must be taken into account.

**Peridental Infection.**—Acute inflammation results from the action of virulent staphylococci, streptococci, and other organisms, when they gain access to tissues about a tooth, beside it, beneath it, or within its pulp. A

dead tooth may be judged always to be infected. It may unexpectedly flare with violent inflammation, so that acute cellulitis with abscess makes its appearance. Trauma, loosening the tooth, is a common incitation to infection. Caries may let in pathogenic bacteria. The type of infection and the individual's response to it determine the clinical course. Staphylococci may be expected to produce acute purulent cellulitis, which localizes, results in abscess, and then may safely be incised and drained. Some staphylococci are dermonecrotic, so that the cellulitis is a sloughing one. This may appear as a complication of debilitating or exanthematous diseases, and prove fatal. It is as dangerous as carbuncle of the face. Streptococci may provoke superficial gingivitis, erysipelas, purulent cellulitis, diffuse and burrowing cellulitis, and sloughing lesions. Response to penicillin or sulfonamides if appropriate is gratifying but abscesses have to be drained adequately

**Pyorrhea Alveolaris**—The gingival trough deepens and eventually extends into the periodontal space thereby forming slowly growing pockets, lined with epithelium. The trough collects débris of food, detritus of exfoliation and exudation, calculus, and the agents and products of fermentation. With discontinuity of the epithelial barrier inflammatory reaction may become either suppurative or granulomatous. The process extends toward the roots of the tooth so that the tooth is loosened its sides bathed with pus or encased with granuloma. Three clinical types of involvement are described

MARGINAL PYORRHEA ALVEOLARIS, with chronic purulent gingivitis and superficial pocket formation;

DIFFUSE PYORRHEA ALVEOLARIS, with deep pocket formation, suppuration, and loosening of the teeth; and

PRECOCIOUS SENILE ALVEOLAR ATROPHY which is often associated with deep pocket formation.

Acute pyogenic infection of a pyorrheic pocket may occur with the formation of an abscess and eventual discharge by perforation or by incision and drainage

*Pyorrhea eventually heals itself the gums receding the teeth falling out* and the sockets healing with scar Pyorrhea is of importance as a focus of infection for it harbors streptococci (Cokkinis BMJ 2 1158, 1939) Its significance in internal medicine was stressed by Miller and Arvins (NYSJM 41 359 1941) who noted that in periodontia the area of absorption is considerably greater than in a mere root abscess. Dermatoses frequently related with pyorrhea as a focus of infection are, in our opinion sycosis barbae lupus erythematosus, lichen planus, pustular acrodermatitis, and chronic ulcer of the leg Even syphilis and psoriasis respond better to treatment when the mouth is medically clean. To cure pyorrhea Webb (Dental Survey Aug 1930) advised destruction of gingival tissue external to the pockets with fulguration so providing adequate drainage. In severe pyorrhea, extraction is the only successful measure.

**Focal Infection.**—In chronic quiescent, peridental infection, staphylococci or streptococci or both may be present and only inconspicuously active Yet they are absorbed into the circulation in small numbers from time to time, and like other particulate matter in the circulation tend to be filtered out at sites of inflammation Thus incidental benign cutaneous inflammation, occurring in a person with a focus of infection may become chronic dermatitis which manifests flares and recessions, and which responds un

satisfactorily or not at all to local applications (Duke Oral Sepsis, Mosby 1918) There are cases of chronic, recurrent pustular dermatitis, particularly of the hands and feet, which can be cured only after foci of infection, especially oral foci, have been eradicated. Persistent bullous eruptions resembling staphylococcic impetigo were observed by Epstein (ADS 56 452, 1947) and could not be cured until dental foci were eliminated.

**Noma.**—Any gangrenous, oral infection is called noma (Eckstein AmJDisChild 59 219, 1940) Dermatology and stomatology afford point for point analogies. While the mouth normally harbors a luxuriant flora, it is harmless, as skin flora is harmless, until a locus minoris resistentiae is offered or until a virulent pathogen is introduced into the equilibrium.

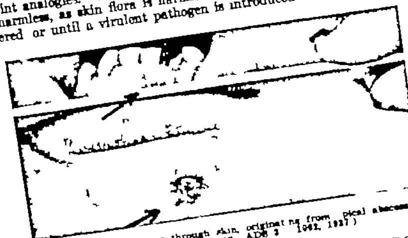


Fig. 1045—Sinus tract, pening through skin, originat ng from pical abscess f lower incisor tooth. (Anderson ADS 3 1062, 1937)



Fig 1046



Fig 104

Fig 1046—Periadenitis mucosa necrotica recurrens, involving buccal surface of upper lip (Hayes, I, V Clin cal Diagnosis f Diseases f the Mouth Dental Items of Interest Publishing Co Inc)

Fig. 1047 – Recurrent scarring philis m ol ing tongue

Devitalization of the mouth tissues from chemical injury chronic infection deficient hygiene inadequate diet or avitaminosis is a predisposing caus[e] Agranulocytosis, frequently the result of dermatitis medicamentosa (q v is associated with ulcerative stomatitis, which is also a frequent co[n]comitant of hematopoietic blastoma especially monocytic leukemia (q v Penicillin in adequate intramuscular dosage is the best treatment alo[ng] [wi]th permanganate douches, transfusions if indicated, and attention to [...] as well as the local ones.

**Sinus Tracts of Dental Origin.**—Chronic inflammation about a tooth may lead to exudation and burrowing which may be practically asymptomatic, like a cold abscess. Eventually the sinus tract ruptures through the gum, palate, or skin (Anderson ADS 35: 1062, 1937 Duckworth BJD 52 57 1940 Wendo and Solomon ADS 46 665 1942 Montgomery ADS 41 378 1940) It is cured by extraction of the tooth.



Fig. 1048



Fig. 1049

Fig. 1048 —Geographic tongue (Fox PaMJ 38 463, 1935.)
Fig. 1049 —Geographic tongue (Dr George M. McKee.)



Fig 1050



Fig 1051

Fig 1050 —Black hairy tongue.
Fig. 1051 —Filaments from black hairy tongue (Dr Fred Weidman.)

**Periadenitis Mucosa Necrotica Recurrens (Recurring Painful Scarring Aphthae)** —A lesion commences as a small inflammatory nodule beneath the mucous membrane of the lip cheek or tongue. The lesion gradually increases in size After a few days sloughing occurs, and a solid, mummified looking plug separates, leaving a crateriform depression I ain

is extreme The lesions heal in a week or two, leaving soft, grayish scars. The lesions are usually single, but 2 or 3 may be present at one time. Recurrence is the rule and the course extends over a period of years. The cause is unknown (Sutton JCutDis 29 65, 1911) Sulfathiazole temporarily helped two cases of ours (Sutton J 117 175 1941) and failed in a third. X ray therapy was beneficial to some degree in the case of Fergusson (BJD 51 32, 1939) Repeated vaccinations with smallpox vaccine seemed to account for 6 months of freedom from recurrence in Roncheso's (ADS 56 553 1947) Such cases are extremely recalcitrant to therapeutic effort.

**Cyclic Buccal Ulceration** is comparatively painless, and the lesions heal without scars. The patients are females, and the genital mucosae as well as the oral suffer ulceration The patient generally clears during a pregnancy Estrogenic therapy is usually successful (Jones JObGBE 47 557 1940; Pappworth BMJ 1 271 1941 Moseley JClEndocr 1 346, 1941)



Fig. 1032.



Fig. 1033.

Fig. 1032 Lichen planus of buccal mucosa.
Fig 1033 —Smooth tongue of primary anemia.

**Black Tongue (Hairy Tongue)** is comparatively rare. It is characterized by yellowish, brownish, blackish, or bluish discoloration of greatly hypertrophied papillae in the midline region of the dorsum of the tongue (Ivy USNMBull 24 16 1926) The malady may develop quickly or slowly The duration is variable. Symptoms are usually absent. Heldingsfeld (J 4 2117 1910) was convinced that a parasitic cause could not be established. Perhaps inflamed, acanthotic and elongated filiform papillae become dark by oxidation, as comedones do. Kennedy and Howles (ADS 42: 666 1940) thought monilia to be etiologically concerned. The disorder is harmless. Potassium chlorate 0.3 gm t.i.d. cured a patient of Tomb (JTropM 43 156 1940) Skillfully applied, an escharotic such as trichloracetic acid or 15 per cent salicylic acid in glycerol (Marshall AnnOtol 49 961, 1940) is curative.

**Transitory Benign Plaques of the Tongue (Geographic Tongue)** is a recurring inflammatory disorder characterized by almost asymptomatic

superficial, circinate, migratory lesions which pursue an acute course, disappear and recur at irregular intervals. The affection is fairly common, but its cause is unknown (Greenbaum: ADS 39 686 1939) Treatment usually proves futile or irritating although Shaw (ADS 56 110 1947) reported relief with a penicillin mouthwash, 1 000 units per c.c. in saline.

**Chronic Superficial Excoriation of the Tongue (Moeller's Glossitis)** is a chronic inflammatory disorder of the tongue, affecting particularly the sides and tip characterized by the formation of irregular usually sharply defined intensely red spots in which the papillae appear thin and swollen. The areas never become ulcerated. They exhibit a slight tendency to extend laterally but persist in the same size and outline despite all treatment. Some patients complain of severe and persistent burning and in others there are paroxysmal attacks of lancinating pain. The ingestion of acids and highly spiced foods usually gives rise to great discomfort. There is no disturbance of appetite or of taste, although eating is torturous. It is possible that cases called Moeller's glossitis fall into 5 classes stomatitis venenata, stomatitis due to systemic allergy as in drug eruptions, stomatitis due to nutritional deficiency glossodynia due to neural disturbance, and finally true Moeller's glossitis, of which the cause is not known (Rattner ADS 55 463 1947) The disease is not rare, but it is extremely difficult to relieve. Estrogenic substances deserve trial

**Lingual Tonsillitis.**—The lingual lymphadenoid tissue, ordinarily anatomically inconspicuous, may become acutely or chronically inflamed. The lymphoid tissues at the sides of the base of the tongue opposite the lower third molars, are the ones usually involved. Occasionally the whole row of lymphatic nodules across the tongue in the region of the circumvallate papillae is affected (Waldapfel AOtol 30 269 1939) The complaint is of persistent irritation, symptomatic during mastication and swallowing One finds a lesion consisting of a group of soft, reddened, rounded papules, which may be fissured or excoriated. One must differentiate syphilis, tuberculosis, and carcinoma. While sulfonamides or penicillin might do the job we have not as yet used them, and destruction performed by means of the actual cautery is curative (Hollander J 102 1151 1934

**Lingual Papillitis.**—Solitary and isolated lingual papillae at times become the site of acute and evanescent simple inflammation. Momentary unipolar electrodesiccation without anesthesia is curative (Scholtz ADS 32 601 1935)

**Granuloma Pyogenicum** (q v ) may affect any part of the mouth. Dental granulomas and many epulides are really granuloma pyogenicum The lesions are generally soft deep red, easy to bleed, and pedunculated. Arising from the gingiva, a pyogenic granuloma is practically invariably associated with granuloma of the root of the tooth underlying It cannot then be got rid of permanently except by extracting the tooth and scraping the socket.

**Granuloma Fissuratum** is a peculiar circumscribed, firm whitish, fissured, granulomatous new growth occurring in the labio-alveolar fold. The lesions are discoid smooth, rounded, and slightly raised. They are about a centimeter in diameter lack an inflammatory areola, and are folded like a bent coin so that the fissure in the bend is continuous at both sides with the labioalveolar sulcus. Symptoms are slight. These benign, fissured nodules represent inflammatory reaction in buccal tissue to a

fissure, possibly of traumatic or streptococcic origin, which is mechanically delayed in healing (Sutton ADS 26 42, 1932 Kingery and Illge JLancet 50 485 1936) In diagnosis, carcinoma must be excluded. Excision is curative perhaps conservative methods may prevail.

**Fissures of the Lip** of shallow extent and comparatively minor significance generally accompany contact and actinic cheilitis, and respond to appropriate treatment of the underlying condition. One sometimes sees a solitary fissure, chronic painful and stubborn, due usually to the streptococcus. Sulfonamide or penicillin is often curative.

**Specific Local Infections in the Mouth.**—Impetigo may extend upon the lips. Erysipelas, diphtheria, tuberculosis, glanders, tularemia, anthrax, rhinoscleroma, syphilis, yaws, leishmaniasis, actinomycosis, sporotrichosis, cephalosporiosis, and rhinosporidiosis are specific infections with oral manifestations. Coccidioidal granuloma produces oral lesions, especially in cases with a grave prognosis. See also histoplasmosis and granuloma inguinale.



Fig. 1054.



Fig. 1055.

Fig. 1054.—Granuloma fissuratum, typical fissured lesion in lower labioalveolar fold. (Sutton ADS 26 665, 1932.)

Fig. 1055.—Granuloma fissuratum sectioned across the fissure, showing inflammatory structure and intense polymorphonuclear leucocytic inflammation about the fissure itself (Sutton ADS 26 426 1932.)

Virus Diseases affecting the mouth include herpes simplex and herpetic aphthous stomatitis, q.v p. 123.

Warts of the mucous membranes are not consequentially different from filiform and ordinary warts (Howarth Laryng 50 23, 1935) Vulvar warts respond to podophyllin, which we are reluctant t put into the mouth.

Molluscum Contagiosum may occur rarely on the lips or in the mouth.

Aphthae.—These lesions, commonly called canker sores, are acute circumscribed, inflammatory lesions which may be recurrent and which occur transiently either singly or in small numbers. The first stage is a tiny vesicle which enlarges a little and becomes eroded. The resulting soft, painful, flat shallow ulcer is rarely wider than a few millimeters. It floor is grayish white and fibrinous and its narrow areola is brightly inflamed. Fetor is not a notable feature The duration of a lesion from its inception to its spontaneous healing is likely t be about a fortnight. No scar ordinarily results. The cause is unknown. Chocolate and nuts, particularly walnuts and pecans, are provocative in some person Recurrent aphthous stomatitis may represent recurrent lesions of chronic herpetic infection. The ulcer may be touched with silver nitrate stick.

Herpetic Stomatitis, highly infect ve but benign and uncomplicated disease occurs sometimes in epidemic form (Dodd et al. JPed 12 95 1938; Breese AmJ DisChild 61: 673, 1941; Scott et al. J 117 999, 1941) The incubation period is

from 5 to 7 days, and fever is marked. Vesicles appear and become ulcers on the fauces, palate, and tonsils, and undergo evolution and healing in due time. Burnet and Lush (Lancet 1: 629 1939) concluded that aphthous stomatitis in infancy is the common manifestation of primary infection with herpetic virus. We regularly cure recurrent herpes about the mouth by removing foci of infection, including malplaced third molars with pockets beneath them, and by giving smallpox vaccine intracutaneously (Woodburne: ADS 43: 543 1941)

GONORRHEAL STOMATITIS is seen in the newborn as an exceptional manifestation of birth canal infection, much less common than gonorrheal ophthalmia. The tongue and palate show yellow white patches with acute inflammation diagnosed by smears and cultures and curable with penicillin.

THRUSH (moniliasis, q.v.) is frequently exemplary of oral infection of the newborn with vaginal plant life. See Plass et al. (AmJOG 21: 321, 1931) Waters and Cartwright (J 113: 10 1939)

STREPTOCOCCIC GINGIVITIS.—Streptococci may cause acute or chronic, transient or persistent, and moderate or violent disease of the oral mucous membrane or deeper tissue They particularly favor the lymphoid tissue of the mouth for their habitat, finding pyorrheic pockets, dead teeth, and paradental abscesses also suitable foci. They may cause erysipelas, burrowing ulcer and scarlet fever as severe, acute infections. Less severe is a typical form of hypertrophic gingivitis due to *Streptococcus viridans*. Outstanding features are swelling pain, and redness of the gums, palate and throat. The disease is acute in onset, and it is accompanied by fever salivation, and malaise. The soft gingival margins are bright red, rolled and edematous, the papillae being pushed up between the teeth. There is no ulceration erosion, vesiculation, or membrane formation. The disease generally responds within a week to treatment with local antiseptics and sulfonamide drugs (Woodburne: JMichSMS 34 384, 1935)

VINCENT'S DISEASE is an acute, ulcerative infection of the mucous membranes, attributed to a combination of fusiform bacillus and spirochete (Vincent: AnnInst Pasteur 10 488, 1896; 13: 609 1899) Trench mouth, as it is called is characterized usually by the development of painful, superficial ulcers, covered with an adherent greenish-gray membrane. There i usually some fever and the submaxillary and cervical lymph nodes are swollen and painful. The mouth has a strongly fetid odor Sali tion is copious. Swallowing and eating are painful, almost impossible. The lesions spread rap lly The disease is usually acute in onset and its course is severe. F tality is unusual but Henry (BMJ 1: 1104 1936) reported deaths. Spontaneous healing may be expected after a few weeks, but response to treatment is usually prompt. Superficial diphtheroid cases and ulcerative types are seen. Violent infection may supplant mere hallow ulcerat on so that noma supervenes.

Venereal fusospirochetosis produces progressive and destructi e ulceration of the external genitalia w th cop ous purulent, sanguineous discharge and notable fetor (von Hamm AmJTropM 18: 595 1938) Vincent's balanitis was manifested with superficial yellow ulcers, grayish preputial erosions, and phimosis in the case of Thomson (BMJ 453 1943)

Chronic Vincent s infection is believed to be comparatively common; certainly chronic ulcerat gingivitis occurs and in the lesions Vincent s organisms are numerous. The organ sms in uch cases are at least sometimes merely secondary invaders, and the underlying difficulty may range from stomatitis of malnutrition to that of contact stomatitis or medicinal injury

Skin infections occur Some cases have followed bites or from striking fists against teeth. The lesion becomes an ulce with putrid odor and greenish slough. Erythematous patches bulla and hallow ulcers were seen on the skin in 7 cases affecting the mouth severel and w th fatal outcome, reported by Goldman and Kelly (J 101 339 1933) Onychia and paron hia were reported by Benedek, Surg 11 5 194 ) and purulent paronychia with ulceration beneath the toes was observed by Strickler (ADS 5 87 1945)

Trench mouth is an infection and is tran mis ble Vincent organisms are present in almost all mouths n the interdental crevices and the gingival trough. When circumstances are f orable they multiply promptly Pellagra, scurvy and other tritional disturbances pred pose to, and complicate, Vincent s angina (Williams: Tex SJM 34: 779 1939) The problem f the pathogenic ty f oral organisms i still cloudy Vincent's d sease may be virus infection the fusosp rochet l organisms being only incidental (Black J I ed 70 143, 194.)

Vincent's disease m t be d fferentiated from diphtheria, especiall ton llitis, agranulocytic angina l ph l The pa lcers, membranes fetor acute course

of the disease, and adenitis are typical. The symptoms to which it gives rise are distressing and by continued extension of the involved area an attack may extend over a period of many weeks.

In treating Vincent's angina arsphenamine intravenously has been recommended as a specific, but it is not. We have seen severe dermatitis following the use of arsenicals in this local condition, which has been known to appear during antisyphilitic treatment (Sutton: J 83: 1919 1924) When topically applied the aqueous or glycerinated solution of neoarsphenamine is valuable (Rosebury et al.: JInfectDis 65: 291 1939) Locally hydrogen peroxide or sodium perborate as a damp paste is useful. The mouth must be kept clean by gentle measures, and dental hygiene and prophylactic treatment are indicated in the chronic cases. No immunity develops; the disease becomes worse if untreated. Sulfanilamide helps, and nicotinic and ascorbic acids may be needed. Fuadin intravenously for 6 to 12 injections was recommended by Smith (BMJ 35: 299, 1942) Since penicillin became available, other treatment has largely been set aside. *The intramuscular injection of large doses is extremely effective (Sweeney et al.: JLCM 30: 122, 1945; Joseph: BMJ 38: 778, 1945; Pearce and McDonald J 128 343, 1945)* Penicillin lozenges (Page and Lipman ValMonth 73: 490 1946) or sprayings with 250 units per c.c. (Strong and Willett; *USNMBull 46: 853, 1946*) are also efficacious.



Fig. 1036.



Fig. 1037

Fig. 1036.—Vincent balanitis (Madd: J 101 420, 1936.)

Fig. 1037.—Fusiform bacilli and Vincent's spirochetes smear from Vincent's angina, *of which such microscopic findings are diagnostic. (Mead: Diseases of the Mouth* Mosby Co.)

## SYSTEMIC DISEASE AFFECTING MUCOSAE

**Symptomatic Stomatitis in Systemic Disease** is common, *for few* systemic diseases fail to manifest oral lesions at least occasionally The following described elsewhere manifest oral symptoms more or less commonly anthrax, chicken pox, coccidioidal granuloma erythema multiforme, herpes zoster of fifth nerve, leishmaniasis, leprosy lichen planus, lupus erythematosus, lymphogranuloma inguinale, measles, moniliasis, pemphigus, smallpox, scarlet fever sporotrichosis, syphilis, tuberculosis, and yaws. See also avitaminosis, *pemphigus, acanthosis nigricans*, eruptive stomatitis, erythema multiforme, etc. (Wood AOtol 36: 650, 1942) Small white specks on the buccal mucosa may be seen in the first few days of influenza (Wolff APed 58 1 1941) Severe angina with purulent

exudate, edema, and hemorrhage have been described in infectious mononucleosis (Smith and Shaw BMJ 1 581 1945)

PURPURA.—Purpuric hemorrhage within the mouth may occur along with purpuric manifestations elsewhere and the causes of oral lesions, which may be symptomatically conspicuous in thrombocytopenic purpura, comprise all the causes of purpura (p 451) Hemophilia, leukemia, hereditary telangiectasis, epilepsy vicarious menstruation, and pulmonary and esophageal diseases must be considered in bleeding from the mouth.

AGRANULOCYTOSIS.—Angina is a major symptom of neutropenia. Necrotizing inflammation of the tissues of the throat may accompany neutropenia of any cause including aplastic anemia. Among the drugs which may cause neutropenia are acetanilid, amidopyrine arsenicals, barbiturates, benzene, cinchophen, quinine, Sedormid, and the sulfonamides.

The destruction of leucocytes may at times be due to allergy so that thrombocytopenic purpura and agranulocytosis are related. Much benefit was obtained with penicillin in the 2 cases caused by Mapharsen reported by Smith et al. (J 126 1027 1944) Arsenical and gold poisonings with *agranulocytosis are responsive to BAL*

**Allergic Stomatitis.**—Distinguishing systemic allergy from contact mucositis, we call attention to urticaria and angioneurotic edema (p 105) and drug eruptions (p 88) Drugs which often affect the mouth include bismuth (Webb SMJ 34 1136 1941) chromates, gold phosphorus (Heimann JIndustHyg 28 142, 1946) iodides, and all of those which may cause agranulocytosis or purpura.

## METABOLIC DISEASES

The mouth is affected more or less considerably in the following diseases, most of which are described elsewhere.

Acanthosis nigricans Pigmentation and papillation of the mouth occur
Acromegaly Bony distortion malposition of teeth macroglossia.
Amyloidosis In systemic amyloidosis, glossitis is usually prominent.
Avitaminosis B See pellagra, pernicious anemia, ariboflavinosis, and perlèche.
Hunterian glossitis and glossitis of iron deficiency are described separately
Avitaminosis C is scurvy
Diabetes mellitus and insipidus may cause xerostomia or avitaminotic stomatitis.
Hyperparathyroidism results in cystic tumors of the jaw malocclusion, and distortion and hypermobility of the teeth (Strock NEngJM 224 1019 1941)
Hypogonadal states in the climacteric or in castrates may be associated with dry burning mouth with leukoplakia and fragility of the mucosae pallor and epidermal atrophy all responsive to estrogenic therapy (Richman and Abarbanel JClEndocr 3 224 1943)
Menstruation is sometimes accompanied by oral changes. Vicarious menstruation, with bleeding from the gums and elsewhere instead of from the uterus has been seen. In menstrual relationship there may occur salivation, aphthae toothache herpes, and erosion of the lips.
Myxedema Thickening and enlargement of the tongue and lips are seen.
Polycythemia ... burning and tenderness of the lips and mouth.
Pregnancy
Marginal gingivitis generally more marked about the lower front teeth, is common Rapidly advancing dental caries may result from decalcification.
Gingivitis of pregnancy begins about the second month of gestation and lasts until the termination of it and longer perhaps.
Fungoid growths of the gingival papillae are seen. Epulis may develop and luxuriate

Hypertrophic gingivitis of pregnancy is a recognized clinical condition, swelling and diffuse hypertrophy becoming marked with the onset of mammary changes during the fourth month (Schmitt ADS 40: 654, 1939; Ziskin: JDentRes 16: 367 1938) Edema, fibrosis, tenderness, and a degree of fragility which makes bleeding easy are characteristic, and may be extreme. Inflammatory tumors may develop during pregnancy

Scleredema The tongue may be affected.

Scleroderma: Oral involvement may be serious in generalized cases affecting the head, interfering with deglutition.

Uremia has been reported to cause membranous stomatitis (Bereston and Keil: ADS 44: 562 1941)

Xanthoma: Xanthomatous infiltration of the gums may be marked (Cohen and Fisk: J Lancet 59: 19* 1939)

**Hunter s Glossitis.**—In severe anemias and sprue the tongue is sometimes so atrophic that it weighs only 60 per cent of the normal amount, and this is due to diminution in the quantity of muscular tissue as well as to superficial atrophy Anemia is obscured in many cases by the redness of inflammation. The mucosa and submucosa may harbor *Streptococcus viridans* In pernicious anemia, atrophy of the papillae of the tongue is typical, affecting the sides particularly and the redness of the inflamed lingual mucosa stands in contrast to the pallor of the remainder of the mouth. Burning and stinging sensations at the borders and at the tip of the tongue are common complaints. Stomatitis of pernicious anemia is symptomatically benefited by successful antianemic treatment, which must include an ample supply of B complex, especially folic acid, q v Secondary anemia of the sort benefited by large doses of iron is associated also with glossitis (Darby J 130 830 1946) Alcoholism causes glossitis which is identical with that of pellagra (q v ) and proper diet and nicotinic acid are promptly effective. Stomatitis in avitaminotic states was discussed by Topping and Fraser (PHRpts 54 416 1939) and Manson Bahr (Lancet 2 317 356 1940) Lack of pyridoxine caused sore tongue in the case of Rosenblum and Jolliffe (J 117 2245 1941)

**Pernicious Anemia.**—The tongue may become beefy red smooth, and painful, the process usually commencing at the margins. This may be an early symptom. Eventually it becomes smooth and atrophic. See avitaminosis, folic acid (p 440)

**Diabetic Stomatitis** is characterized by the deep red color and extreme dryness of the mucosa. The tongue is likely to be swollen, showing indentations of the teeth at its margins. Rigid oral hygiene is essential, and one may prescribe mild alkaline mouthwashes Metabolic balance must be obtained.

**Foetor Oris ( Halitosis )** is almost always due to local causes although it has been proved that odorous substances can circulate through the blood and so reach the lungs, to be exhaled in recognizable concentration (Crohn and Drosd J 117 2242, 1941) Objectionable odors arise usually from stagnation and fermentation of food débris in the mouth. Bad hygiene, calculus, pyorrhea and decay abet this. The odor of fermenting blood serum may result from too strenuous efforts to keep the mouth clean Tonsillar crypts may contain odorific caseous material and nasopharyngeal troubles may be the source Metabolic disturbances such as scurvy purpura, uremia, diabetes, cirrhosis of the liver acne, hunger fatigue menstruation, and intoxications of various sorts modify the smell of the breath Cases require and justify careful consideration They are usually responsive to suitable treatment, unless the patient,

having read the ads, is only imagining things. See Drosd and Crohn (AmJDigDis 9 79 1942) and Buccal cacosmia (J 111 1968 1938 113 2170 1939) See also Bromidrosis, p 689

## PIGMENTATION

Normal pigmentation of the mucous membrane is comparable with that of the skin melanophores and dopa positive cells being numerous in the oral mucosa (Becker ADS 16 259, 1927) A list must suffice, here, of disturbances of pigmentation as seen in the mouth see Castor (JTropM 15 117 1912) and Monash (ADS 26 139 1932) Pigment may be melanin hemosiderin, or other substances, such as deposits of metals tattoo of the mouth occurs depigmentation as well as hyperpigmentation may take place and the color of the blood affects the color one sees

Acanthosis nigricans and Addison s disease cause oral melanosis.
Anemia. Pallor of the mucosae may be notable.
Arsenical pigmentation may affect the mouth as well as the skin.
Avitaminosis. Pellagra and hypothyroidism may be accompanied by mucosal hyperpigmentation.
Black tongue, described elsewhere.
Blue gum, normal pigment occurring in Negroes.
Carbon monoxide poisoning Mucosae appear brighter red than normal.
Cyanosis.
Jaundice
Leucoplakia alters the color of the site.
Melanoma may occur in the mouth.
Melanoplakia is the name applied to pigmentary spots possibly existing normally sometimes appearing with leucoplakia superimposed on them.
Metal deposits, including bismuth, lead, silver mercury
Methemoglobinemia, caused by various drugs. The mucosae become blue.
Normal pigmentation is variable and may be spotty
Polycythemia causes purplish redness of the mucosae.
Quinacrine causes slate blue spots occasionally
Tattoo of the tongue or gums, with ink or charcoal.

## NEUROSES

**Burning Tongue Glossodynia.**—The patients are generally of middle age and most of them are women The tongue gives rise to exceedingly distressing symptoms, described as if it had been scalded The front half of the tongue and the sides are generally mainly affected. Rarely it is unilateral and sometimes the side of the cheek or of the lip may be affected too There is no visible alteration of the mucosa The cause is not known (Engman ADS 1 137 1920 Fox NYSJM 35 881 1935) The symptoms are continuous and are severely annoying The disturbance may continue without change whether treated or not over a period of years (Gilpin J 106 1722, 1936) Lingual tonsillitis is a cause of abnormal sensations in the tongue it is not a cause of true burning tongue Amyloidosis (q v ) is a cause of enduring and incurable lingual distress. Buccal neuralgia may be the equivalent of migraine in some instances or tic douloureux in others (Reichert Surg 41 473 1940) Glossodynia leads to cancerophobia and reassurance has some utility

Disturbance of the temporomandibular joint may provoke lingual symptoms by irritating the auriculotemporal nerve and chorda tympani so that relief may be obtained by adjusting dentures and so correcting joint function. When molars are ground low by attrition or when prostheses are not high enough, the jaws may close so as to pinch the nerve

**Neural Lesions of the Mouth.**—Peripheral lesions of the ninth nerve cause loss of taste on that side in the anterior two-thirds of the tongue. Integrity of the facial nerve, vulnerable in various ways, is important for normalcy of the mucosa of the lips and cheek on that side, and also of the conjunctiva. Bulbar palsy syphilis, poliomyelitis, and syringomyelia may cause atrophy of the tongue by damaging the twelfth nerve which supplies lingual motor innervation (Costen's syndrome; see Bell MJAustral 2 433 1946, Emenheiser OklaSMAJ 32 256 1939) Buccal neuralgia may require division of the facial artery vein and sympathetic nerves (Reichert ASurg 41 473 1940) or injection of the mandibular branch of the trigeminal nerve.

**Glossalgia.**—Tic douloureux of the ninth cranial nerve, affecting the oral mucosa and tongue occurs (Hoover and Poppen J 107 1015 1936) Herpes zoster may appear within the mouth. Unilateral tingling and paroxysmal pain in the mouth were cured in three cases of ours by intra cutaneous smallpox vaccination (compare segmental neuralgia)

**Psychotic Disorders.**—Sucking the tongue, chewing the mucosa of the cheeks or lips, compulsion neuroses involving weird manipulations of the organs of the mouth and oral erotism deserve mention. Cancer ophobia, often grounded upon the patient s discovery and misinterpre tation of lingual tonsillar tissue or circumvallate papillae is a disorder the stomatologist may treat.

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**Contact Mucositis.**—*Loveman (ADS 37 79, 1938)*; Templeton and Lunsford (ADS 25 439, 1932) toothpaste Woodburne (JMichSMS 39 407, 1940) Miller (J 116 131, 1941) cinnamon in chewing gum Silvers (J 116 2257 1941) *rhus toxicodendron*, also anal Goldman (ADS 53 124, 1946) penicillin mouthwash Brown (SMJ 31 164, 1941) conjunctivitis.

**Leukoplakia.**—McCarth (ADS 34 612 1936) N thruson nd Weisberger (NEngJM 221 884, 1939) treatment with estrogen Orr (Lancet 2 575, 1933), betel nut cancer; Sparrow (AmSurg 112 37 1940), vulvar Sturgis and Lund (NEngJM 210 996, 1934) Vickers et al (SouthSurg 8 [illegible], 1939) anal; Meyer (SGO 73 139 1941) cervix, Pund and Auerbach (J 131 960 1946), cervix; Hyams and Bloom (AmJOG 53 214 1947) vulva treatment with vitamin A and HCl Eichenlaub (ADS 37 [illegible], 1938) Hagen and Eichenlaub (J 79 1487 1922); Thompson and Stein (JUrol 44 [illegible], 1940) bladder Crowell (PDMChi 13 [illegible], 1940), renal pelvis.

**Miscellaneous Oral Lesions.**—De [illegible] (BJD 51 177 1939) periadenitis necrotica, Holter and Middleton (J 102 2303, 1933) smooth tongue; New and Childrey (AOtol 12 161, 1930) blastomycosis of tongue; Thompson and Montgomery (J 93, 114, 1939) black tongue Tobias (InternatClin 3 92, 1937), syphilis Tomlinson (PHRpts 54 [illegible] 1939) a [illegible] Wakeley nd [illegible] (Lancet 1 748, 1939), palatal herpes; Levine et al. (J 112 2020, 1939) epidemic aphthae Pusey (J 114 1514, 1940) denture influence on taste sensibility

**Salivary Gland Diseases.**—Furstenberg (J 130 1, 1946)

**Vincent's Disease.**—Brunsmle nd Greene (Re[illegible] 20 1940) incidence of organisms King (Lancet 2 32, 1940) [illegible] therapy Smith (Fusospirochetal Disease, Williams and Wilkins, 1932)

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